



(10) International Publication Number
WO 2005/019446 A2

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(57) Abstract: The invention relates to novel forms of protein tyrosine phosphatase enzymes and methods of using such enzymes to identify agents or compounds capable of altering or modulating the activity of the native protein tyrosine phosphatase.

WO 2005/019446 A2

NOVEL FORM OF PROTEIN TYROSINE PHOSPHATASES AND METHODS FOR
IDENTIFYING MOLECULES BINDING THERETO

CROSS-REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. Provisional Patent Application
5 No. 60/476,036 filed June 4, 2003, which is incorporated herein by reference in its
entirety.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR
DEVELOPMENT

This invention was made with government support under Grant No. R01-
10 GM55989 and Merit Award R37-CA53840 awarded by the National Institutes of Health.
The government may have certain rights in this invention.

TECHNICAL FIELD

The present invention relates to the protein tyrosine phosphatase family of
enzymes that mediate biological signal transduction, and in particular to novel forms of
15 such phosphatases, and to assays using such novel protein tyrosine phosphatases.

BACKGROUND OF THE INVENTION

Reversible protein tyrosine phosphorylation, coordinated by the actions of
protein tyrosine kinases (PTKs) that phosphorylate certain tyrosine residues in
polypeptides, and of protein tyrosine phosphatases ("PTPs") that dephosphorylate certain
20 phosphotyrosine residues, is a key mechanism in regulating many cellular activities. It is
becoming apparent that the diversity and complexity of the PTPs and PTKs are comparable,
and that PTPs are equally important in delivering both positive and negative signals for
proper function of cellular machinery. Regulated tyrosine phosphorylation contributes to

specific pathways for biological signal transduction, including those associated with cell division, proliferation and differentiation. Defects and/or malfunctions in these pathways may underlie certain disease conditions for which effective means for intervention remain elusive, including for example, malignancy, autoimmune disorders, diabetes, obesity and
5 infection.

The protein tyrosine phosphatase family of enzymes consists of approximately 100 structurally diverse gene products that have in common a highly conserved amino acid PTP catalytic domain, but which display considerable variation in their non-catalytic segments. In particular, the "classical" PTPs, exclusively catalyze
10 dephosphorylation of (and thus exhibit specificity for) phosphotyrosine residues in phosphoproteins and phosphopeptides, in contrast to the "dual specificity phosphatase" (DSP), members of the PTP family that are capable of dephosphorylating phosphotyrosine as well as phosphoserine and phosphothreonine residues in substrate phosphopolypeptides. This structural diversity presumably reflects the diversity of physiological roles of
15 individual PTP family members, which in certain cases have been demonstrated to have specific functions in growth, development and differentiation (Desai et al., 1996 *Cell* 84:599-609; Kishihara et al., 1993 *Cell* 74:143-156; Perkins et al., 1992 *Cell* 70:225-236; Pingel and Thomas, 1989 *Cell* 58:1055-1065; Schultz et al., 1993 *Cell* 73:1445-1454). PTPs participate in a variety of physiologic functions, providing a number of opportunities
20 for therapeutic intervention in physiologic processes through alteration or modulation (e.g., statistically significant up-regulation or down-regulation) of PTP activity.

Although recent studies have also generated considerable information regarding the structure, expression and regulation of PTPs, the identities of some of the tyrosine-phosphorylated substrates through which the PTPs exert their effects remain to
25 be determined. Studies with a limited number of synthetic phosphopeptide substrates have demonstrated some differences in the substrate selectivity of different PTPs (Cho et al., 1993 *Protein Sci.* 2: 977-984; Dechert et al., 1995 *Eur. J. Biochem.* 231:673-681; Ramachandran et al., *Biochemistry* 31:4232-38 (1992)). Analyses of PTP-mediated dephosphorylation of PTP substrates suggest that catalytic activity may be favored by the

presence of certain amino acid residues at specific positions in the substrate polypeptide relative to the phosphorylated tyrosine residue (Ruzzene et al., 1993 *Eur. J. Biochem.* 211:289-295; Zhang et al., 1994 *Biochemistry* 33:2285-2290). Thus, although the physiological relevance of the substrates used in these studies is unclear, PTPs display a certain level of substrate selectivity *in vitro*. The family of PTPs can be subdivided into two categories: the classical PTPs, which comprise phosphotyrosine (pTyr)-specific enzymes typified by PTP1B and CD45, and the dual specificity phosphatases ("DSPs") which dephosphorylate pSer/pThr as well as pTyr residues. The DSPs largely maintain the same catalytic mechanism as the classical PTPs and have been implicated in a wide range of fundamentally important signaling events from control of MAP kinases in cell proliferation to the regulation of cyclin dependent kinases in the cell cycle.

The PTP signature motif (Cys-(X)₅-R) (SEQ ID NO:1) is invariant among all PTPs. The cysteine residue in this motif is invariant in members of the family and is known to be essential for catalysis of the phosphotyrosine dephosphorylation reaction. This cysteine functions as a nucleophile to attack the phosphate moiety present on a phosphorylated amino acid residue (*e.g.*, phosphotyrosine, and/or pSer/pThr in the case of a DSP) of the incoming substrate.

For some PTPs, mutation of the catalytic cysteine residue results in a "substrate trapping" mutant PTP that is catalytically deficient but retains the ability to complex with, or bind to, its substrate, at least *in vitro*. (*e.g.*, Sun et al., 1993 *Cell* 75:487). Such signature sequence cysteine mutants of certain other PTP family members, however, do not form stable complexes with substrate. In order to derive catalytically deficient, substrate trapping mutants of such PTPs, instead of substituting serine for cysteine in the CX₅R (SEQ ID NO:1) motif, a wildtype protein tyrosine phosphatase catalytic domain invariant aspartate residue is replaced with an amino acid that does not cause significant alteration of the K_m of the enzyme but that results in a reduction in K_{cat}, as disclosed, for example, in U.S. Patent Nos. 5,912,138 and 5,951,979, in U.S. Application No. 09/323,426, and in PCT/US97/13016 and PCT/US00/14211. (See also, *e.g.*, Flint et al., 1997 *Proc. Natl. Acad. Sci.* 94:1680). Substrates of other PTPs can be

identified using similar substrate trapping mutant PTPs, for example, substrates of the PTP family members PTP-PEST (Garton et al., 1996 *J. Mol. Cell. Biol.* 16:6408), TCPTP (Tiganis et al., 1998 *Mol. Cell Biol.* 18:1622), PTP-HSCF (Spencer et al., 1997 *J. Cell Biol.* 138:845), and PTP-H1 (Zhang et al., 1999 *J. Biol. Chem.* 274:17806).

5 Mitogen-activated protein kinases (MAP-kinases, MAPK) are components of conserved cellular signal transduction pathways that have a variety of conserved members and that are integral to the cell's response to stimuli such as growth factors, hormones, cytokines, and environmental stresses. MAP-kinases are activated via phosphorylation by MAP-kinase kinases at a dual phosphorylation motif that is present in
10 MAPK and that has the sequence Thr-X-Tyr, in which phosphorylation at both the tyrosine and threonine residues is required for MAPK activity. Activated MAP-kinases phosphorylate several signal transduction targets, including effector protein kinases and transcription factors. Inactivation of MAP-kinases is mediated by dephosphorylation of the MAPK Thr-X-Tyr site by dual-specificity phosphatases referred to as MAP-kinase
15 phosphatases. In higher eukaryotes, the physiological role of MAP-kinase signaling has been correlated with cellular events such as proliferation, oncogenesis, development, and differentiation. Accordingly, the ability to regulate signal transduction via these pathways could lead to the development of treatments and preventive therapies for human diseases associated with MAP-kinase signaling, such as cancer.

20 Dual-specificity protein tyrosine phosphatases (dual-specificity phosphatases, or "DSPs"), as stated above, dephosphorylate both phosphotyrosine and phosphothreonine/phosphoserine residues on a variety of substrates (Walton et al., *Ann. Rev. Biochem.* 62:101-120, 1993), including mitogen-activated protein kinases (MAP-kinases, MAPK). MAPKs are a family of conserved cellular signal transduction pathway
25 members that are integral to cellular responses to physiological stimuli (e.g., growth factors, hormones, cytokines, environmental stresses, etc.). More than 50 dual-specificity phosphatases that dephosphorylate and inactivate a MAP-kinase have been identified (Shen et al., *Proc. Natl. Acad. Sci. USA* 98:13613-18 (2001); see also, e.g., U.S. Patent Nos. 6,492,157 and 6,551,810), including MKP-1 (WO 97/00315; Keyse and Emslie,

Nature 59:644-647 (1992)); MKP-2 (WO97/00315); MKP-4, MKP-5, MKP-7, Hb5 (WO 97/06245); PAC1 (Ward et al., *Nature* 367:651-654 (1994)); HVH2 (Guan and Butch, *J. Biol. Chem.* 270:7197-7203 (1995)); and PYST1 (Groom et al., *EMBO J.* 15:3621-3632 (1996)). These dual-specificity phosphatases differ in expression, tissue and subcellular
5 distribution, and specificity for MAP-kinase family members. Expression of certain dual-specificity phosphatases is induced by stress or mitogens, but others appear to be expressed constitutively in specific cell types. The regulation of dual-specificity phosphatase expression and activity is considered to be significant in the control of MAP-kinase mediated cellular functions, including cell proliferation, cell differentiation and
10 cell survival. For example, dual-specificity phosphatases may function as negative regulators of cell proliferation. Very likely, many such dual-specificity phosphatases exist, having varying specificities with regard to cell type or activation state.

In contrast to the role of most dual-specificity phosphatases in the inactivation (*i.e.*, down-regulation) of MAP-kinases, one DSP enzyme, herein referred to
15 as JSP-1 (Jun kinase Stimulating Phosphatase-1) or dual-specificity phosphatase 3 (DSP-3), has been reported to have the capability to function as a selective activator of the JNK MAP-kinase signaling pathway (Shen et al., *supra*; WO 01/21812). DSP-3 appears also to affect the activity of other kinases involved in the JNK pathway (Shen et al., *supra*; WO 01/21812). For example, overexpression of DSP-3 leads to activation of MKK4, a
20 MAP-kinase kinase that functions upstream of JNK (Shen et al., *supra*; Lawler et al., *Curr. Biol.* 8:1387-90 (1998); Yang et al., *Proc. Natl. Acad. Sci. USA* 94: 3004-3009 (1997)).

Activation of JNK is believed to be involved in several physiological processes, including embryonic morphogenesis, cell survival, and apoptosis. A number
25 of JNK signaling pathway substrates have been identified, including c-Jun, ATF2, ELK-1 and others. JNK signaling has also been associated with various disease conditions, such as tumor development, ischemia and reperfusion injury, diabetes, hyperglycemia-induced apoptosis, cardiac hypertrophy, inflammation, and neurodegenerative disorders.

Hence, and as also noted above, over the last fifteen years it has been established that the PTPs are a large, structurally diverse family whose members exhibit exquisite substrate specificity *in vivo* and act as important regulators of a wide array of cellular signaling pathways (Andersen et al., 2001 *Mol. Cell. Biol.* 21:7117; Tonks and
5 Neel, 2001 *Curr. Opin. Cell Biol.* 13:182). An important area of investigation in the field remains the characterization of mechanisms by which the activities of the PTPs themselves may be regulated *in vivo*.

Recently, the art has understood that certain PTPs may be susceptible to site-specific oxidation and consequent inactivation, introducing an additional tier of
10 complexity to the regulation of this family of enzymes. It is now apparent that reactive oxygen species (ROS) are not merely a harmful by-product of life in an aerobic environment. The importance of ROS in physiological activities mediated by phagocytic cells, such as neutrophils, is well documented. Various stimuli lead to the assembly of a multi-component NADPH oxidase complex, which mediates a process known as the
15 respiratory burst (DeLeo et al., 1996 *J. Leukoc. Biol.* 60:677). NADPH oxidase catalyses transfer of one electron from NADPH to molecular oxygen to generate superoxide anions, which in turn may yield hydrogen peroxide, either via protonation of superoxide or through the action of superoxide dismutase (Thelen et al., 1993 *Physiol. Rev.* 73:797). The large quantities of such ROS that are produced in phagocytic cells have been
20 implicated as microbiocidal agents and in certain pathological situations can result in host cell damage (Smith et al., 1991 *Blood* 77:673). However, many recent studies have revealed that the production of ROS is tightly regulated, engendering the concept that, at lower levels than those generated for a microbiocidal function, ROS may also function in propagating a signaling response to extracellular stimuli (Finkel, 1998 *Curr. Opin. Cell*
25 *Biol.* 10:248; Finkel, 2000 *FEBS Lett.* 476:52). Thus, in a manner analogous to reversible protein phosphorylation, the reversible oxidation of target proteins in a cell may regulate the function of those proteins in response to various agonists and thus elicit a cellular response to stimulation (Finkel, 1998).

Several lines of investigation have implicated ROS in the regulation of mitogenic signaling in mammalian cells (Adler et al., 1999 *Oncogene* 18:6104; Brummel et al., 1996 *J. Biol. Chem.* 271:1455-61; Chen et al., 1995 *J. Biol. Chem.* 270:28499; Sundaresan et al., 1995 *Science* 270:296). Mild oxidation can yield a stable sulfenic acid
5 modification of cysteine residues (Cys-SOH) in selected proteins, including a variety of enzymes and transcription factors, which modification has the potential to regulate the function of those proteins (Claiborne et al., 1999 *Biochemistry* 38:15407). In order to understand the role of ROS and redox regulation in the control of signal transduction, it is particularly important to identify the targets of reversible oxidation *in vivo*. In this
10 context, attention has been drawn to the PTPs, which together with the PTKs are responsible for maintaining a normal protein tyrosine phosphorylation status *in vivo*.

The PTPs are cysteine-dependent enzymes that possess the signature motif, -Cys(X)₅-Arg- (SEQ ID NO:1), which forms the base of the active site cleft and contains an invariant cysteine residue (Barford et al., 1995 *Nat. Struct. Biol.* 2:1043). The
15 PTP catalytic dephosphorylation mechanism involves a two-step process, commencing with nucleophilic attack by the S_γ atom of the PTP catalytic site cysteine on the phosphorus atom of the phosphotyrosyl substrate, resulting in formation of a phospho-cysteine intermediate. In the second step the transient phospho-enzyme intermediate is hydrolyzed by an activated water molecule (Barford et al., 1995). Due to the unusual
20 environment of the PTP active site, the pK_a of the sulfhydryl group of this cysteine residue is extremely low (~5.4 in PTP1B, (Lohse et al., 1997 *Biochemistry* 36:4568) and ~4.7 in YOP, (Zhang et al., 1993 *Biochemistry* 32:9340)) compared to the typical pK_a for Cys (~8.5); this low pK_a of the PTP active site cysteine favors its function as a nucleophile but renders it susceptible to oxidation. It has now been shown *in vitro* that
25 treatment with hydrogen peroxide (H₂O₂) of various PTPs (Lee et al., 1998 *J. Biol. Chem.* 273:15366), including dual specificity phosphatases (Denu et al., 1998 *Biochemistry* 37:5633) and low molecular weight PTPs (Caselli et al., 1998 *J. Biol. Chem.* 273:32554), leads to oxidation of the active site cysteine to sulfenic acid. Such oxidation results in

inhibition of activity because the modified cysteine can no longer function as a phosphate acceptor in the first step of the PTP-catalyzed reaction.

Hydrogen peroxide (H_2O_2) is a natural cellular second messenger produced in response to hormones, growth factors and cytokines, and is required for the optimal activation of numerous signal transduction pathways, particularly those mediated by protein tyrosine kinases (Finkel, *Curr. Opin. Cell Biol.* 10:248-53 (1998); Finkel, *Dev. Cell* 2:251-59 (2002); Rhee et al., *Sci. STKE* 53 (2000); available at Internet:http://www.stke.org/cgi/content/full/OC_sigtrans;2000/53/pel); Sundaresan et al., *Science* 270:296-99 (1995); Rao, *Oncogene* 13:713-19 (1996); Bae et al., *J. Biol. Chem.* 272:217-21 (1997); Knebel et al., *EMBO J.* 15:5314-25 (1996)). One mechanism by which H_2O_2 regulates cellular processes is to transiently inhibit PTPs by reversibly oxidizing their catalytic site cysteine residues, thereby suppressing protein dephosphorylation (Knebel et al., *supra*; Mahadev et al., *J. Biol. Chem.* 276:21938-42 (2001); Lee et al., *J. Biol. Chem.* 273:15366-72 (1998)). Oxidation of such cysteine to sulfenic acid is reversible (Claiborne et al., 1999 *Biochemistry* 38:15407), and thus has the potential to form the basis of a mechanism for reversible regulation of PTP activity. In contrast, oxidation by the addition of two (sulfenic acid) or three (sulfonic acid) oxygens to the active site cysteine is irreversible. Interestingly, glutathionylation of the sulfenic acid form of PTP1B has been reported (Barrett et al., 1999 *Biochemistry* 38:6699) and is proposed as a mechanism to protect against further irreversible oxidation and as an important step in the reverse reduction mechanism. Stimulation of A431 cells with EGF was also shown to lead to the production of H_2O_2 and concomitant inhibition of PTP1B (Bae et al., 1997 *J. Biol. Chem.* 272:217). Increased production of intracellular oxidants may therefore contribute to enhanced, tyrosine phosphorylation-dependent signaling, for example in response to growth factors (Bae et al., 1997; Bae et al., 2000 *J. Biol. Chem.* 275:10527; Sundaresan et al., 1995 *Science* 270:296), by transiently suppressing the enzymatic activity of members of the PTP family, thereby promoting a burst of PTK activity (Finkel, 1998; 2000, *supra*).

One non-transmembrane, or intracellular, PTP, PTP1B, recognizes several tyrosine-phosphorylated proteins as substrates, many of which are involved in human disease. For example, therapeutic inhibition of PTP1B in the insulin-signaling pathway may serve to augment insulin action, thereby ameliorating the state of insulin resistance
5 common in Type II diabetes patients. PTP1B acts as a negative regulator of signaling that is initiated by several growth factor/ hormone receptor PTKs, including p210 Bcr-Abl (LaMontagne et al., *Mol. Cell. Biol.* 18:2965-75 (1998); LaMontagne et al., *Proc. Natl. Acad. Sci. USA* 95:14094-99 (1998)), receptor tyrosine kinases, such as EGF receptor, PDGF receptor, and insulin receptor (IR) (Tonks et al., *Curr. Opin. Cell Biol.* 13:182-95
10 (2001)), and JAK family members such as Jak2 and others (Myers et al., *J. Biol. Chem.* 276:47771-74 (2001)), as well as signaling events induced by cytokines (Tonks and Neel, 2001). Activity of PTP1B is regulated by modifications of several amino acid residues in the polypeptide, such as phosphorylation of Ser residues (Brautigan and Pinault, 1993; Dadke et al., 2001; Flint et al., 1993), and oxidation of the active Cys residue in its
15 catalytic motif (Lee et al., 1998; Meng et al., 2002), which is evolutionarily conserved among protein tyrosine phosphatases and dual phosphatase family members (Andersen et al., 2001).

Diabetes mellitus is a common, degenerative disease affecting 5-10% of the human population in developed countries, and in many countries, it may be one of the
20 five leading causes of death. Approximately 2% of the world's population has diabetes, the overwhelming majority of cases (>97%) being type 2 diabetes and the remainder being type 1. In type 1 diabetes, which is frequently diagnosed in children or young adults, insulin production by pancreatic islet beta cells is destroyed. Type 2 diabetes, or "late onset" or "adult onset" diabetes, is a complex metabolic disorder in which cells and
25 tissues cannot effectively use available insulin; in some cases insulin production is also inadequate. At the cellular level, the degenerative phenotype that may be characteristic of late onset diabetes mellitus includes, for example, impaired insulin secretion and decreased insulin sensitivity, *i.e.*, an impaired response to insulin.

Studies have shown that diabetes mellitus may be preceded by or is associated with certain related disorders. For example, an estimated forty million individuals in the U.S. suffer from late onset impaired glucose tolerance (IGT). Patients with IGT fail to respond to glucose with increased insulin secretion. Each year a small
5 percentage (5-10%) of individuals with IGT progress to insulin deficient non-insulin dependent diabetes mellitus (NIDDM). NIDDM and IDDM are associated with decreased release of insulin by pancreatic beta cells and/or a decreased response to insulin by cells and tissues that normally exhibit insulin sensitivity. Other symptoms of diabetes mellitus and conditions that precede or are associated with diabetes mellitus include
10 obesity, vascular pathologies, and various neuropathies, including blindness and deafness.

Type 1 diabetes is treated with lifelong insulin therapy, which is often associated with undesirable side effects such as weight gain and an increased risk of hypoglycemia. Current therapies for type 2 diabetes (NIDDM) include altered diet, exercise therapy, and pharmacological intervention with injected insulin or oral agents
15 that are designed to lower blood glucose levels. Examples of such presently available oral agents include sulfonylureas, biguanides, thiazolidinediones, repaglinide, and acarbose, each of which alters insulin and/or glucose levels. None of the current pharmacological therapies, however, controls the disease over its full course, nor do any of the current therapies correct all of the physiological abnormalities in type 2 NIDDM,
20 such as impaired insulin secretion, insulin resistance, and excessive hepatic glucose output. In addition, treatment failures are common with these agents, such that multi-drug therapy is frequently necessary.

In certain metabolic diseases or disorders, one or more biochemical processes, which may be either anabolic or catabolic (*e.g.*, build-up or breakdown of
25 substances, respectively), are altered (*e.g.*, increased or decreased in a statistically significant manner) or modulated (*e.g.*, up- or down-regulated to a statistically significant degree) relative to the levels at which they occur in a disease-free or normal subject such as an appropriate control individual. The alteration may result from an increase or decrease in a substrate, enzyme, cofactor, or any other component in any biochemical

reaction involved in a particular process. Altered (*i.e.*, increased or decreased in a statistically significant manner relative to a normal state) PTP activity can underlie certain disorders and suggests a PTP role in certain metabolic diseases.

For example, disruption of the murine PTP1B gene homolog in a knock-
5 out mouse model results in PTP1B^{-/-} mice exhibiting enhanced insulin sensitivity, decreased levels of circulating insulin and glucose, and resistance to weight gain even on a high-fat diet, relative to control animals having at least one functional PTP1B gene (Elchebly et al., *Science* 283:1544 (1999)). Insulin receptor hyperphosphorylation has also been detected in certain tissues of PTP1B deficient mice, consistent with a PTP1B
10 contribution to the physiologic regulation of insulin and glucose metabolism (*id.*). PTP1B-deficient mice exhibit decreased adiposity (reduced fat cell mass but not fat cell number), increased basal metabolic rate and energy expenditure, and enhanced insulin-stimulated glucose utilization (Klaman et al., 2000 *Mol. Cell. Biol.* 20:5479). Additionally, altered PTP1B activity has been correlated with impaired glucose
15 metabolism in other biological systems (*e.g.*, McGuire et al., *Diabetes* 40:939 (1991); Myerovitch et al., *J. Clin. Invest.* 84:976 (1989); Sredy et al., *Metabolism* 44:1074 (1995)), including PTP1B involvement in biological signal transduction via the insulin receptor (*see, e.g.*, WO 99/46268 and references cited therein).

An integration of crystallographic, kinetic, and PTP1B-peptide binding
20 assays illustrated the interaction of PTP1B and insulin receptor (IR) (Salmeen et al., *Mol. Cell* 6:1401-12 (2000)). The insulin receptor (IR) comprises two extracellular α subunits and two transmembrane β subunits. Activation of the receptor results in autophosphorylation of tyrosine residues in both β subunits, each of which contains a protein kinase domain. Extensive interactions that form between PTP1B and insulin receptor
25 kinase (IRK) encompass tandem pTyr residues at 1162 and 1163 of IRK, such that pTyr-1162 is brought into close proximity with the active site of PTP1B (*id.*). The presence in IRK of the Asp/Glu-pTyr-pTyr-Arg/Lys (SEQ ID NO:22) motif has been implicated for optimal recognition by PTP1B of IRK. This motif is also present in other receptor PTKs, including Trk, FGFR, and Axl. In addition, this motif is found in the JAK family of

PTKs, members of which transmit signals from cytokine receptors, including a classic cytokine receptor that is recognized by the satiety hormone leptin (Touw et al., *Mol. Cell. Endocrinol.* 160:1-9 (2000)).

Changes in the expression levels of PTP1B have been observed in several
5 human diseases, particularly in diseases associated with disruption of the normal patterns of tyrosine phosphorylation. For example, the expression of PTP1B is induced specifically by the p210 Bcr-Abl oncoprotein, a PTK that is directly responsible for the initial manifestations of chronic myelogenous leukemia (CML) (LaMontagne et al., *Mol. Cell. Biol.* 18:2965-75 (1998); LaMontagne et al., *Proc. Natl. Acad. Sci. USA* 95:14094-
10 99 (1998); Fukada et al., *EMBO J.* 22:479 (2003)). Expression of PTP1B in response to this oncoprotein is regulated, in part, by transcription factors Sp1, Sp3, and Egr-1 (Fukada et al., *J. Biol. Chem.* 276:25512-19 (2001)). These transcription factors have been shown to bind to a p210 Bcr-Abl responsive sequence (PRS) in the human *PTP1B* promoter, located between 49 to 37 base pairs from the transcription start site, but they do not
15 appear to mediate certain additional, independent PTP1B transcriptional events, for which neither transcription factor(s) nor transcription factor recognition element(s) have been defined (*id.*). An enhancer sequence within the PTP1B promoter serves as a binding site for the transcription factor Y box-binding protein-1 (YB-1), which also regulates expression of PTP1B (Fukada and Tonks, *EMBO J.* 22:479-93 (2003)). A correlation
20 was observed between the expression of PTP1B and that of YB-1 in cancer cell lines and in an animal model of type II diabetes (*id.*).

Currently, therefore, desirable goals for therapeutic regulation of biological signal transduction include modulation of PTP-mediated cellular events including, *inter alia*, inhibition or potentiation of interactions among PTP-binding
25 molecules, substrates and binding partners, or other agents that regulate PTP activities. Accordingly, a need exists in the art for an improved ability to intervene in the regulation of phosphotyrosine signaling, including regulating PTPs by altering PTP catalytic activity (preventing or substantially preventing the reversibility of an oxidative event that results in oxidized PTP), and/or by altering PTP binding to PTP substrate molecules, and/or by

altering PTP-encoding gene expression. An increased ability to so regulate PTPs may facilitate the development of methods for modulating the activity of proteins involved in phosphotyrosine signaling pathways and for treating conditions associated with such pathways.

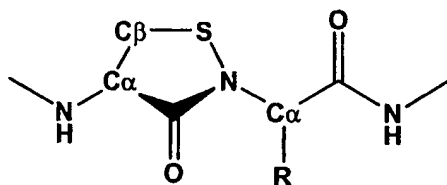
5 Presently, a number of screening assays for agents that regulate PTP activities are known, yet each of these assays has significant limitations, for example, with respect to specificity, sensitivity, or speed. Similarly, poor specificity for PTPs is a shortcoming of certain assays known to the art that, through the use of fluorescence, detect catalytic dephosphorylation of hydrolyzable phosphorylated substrates. Such
10 fluorescence assays employ phosphate esters of fluorescein, for example OMFP (3-O-methylfluorescein phosphate, *e.g.*, Gottlin et al., 1996 *J. Biol. Chem.* 271:27445) or FDP (fluorescein diphosphate, *e.g.*, Huyer et al., 1997 *J. Biol. Chem.* 272:843). These detectable substrates are intrinsically unstable in solution, however, making them poorly suitable for high throughput screening applications. Moreover, PTPs exhibit high
15 specificity for phosphotyrosyl peptide substrates, as noted above, while showing poor specificity for unnatural organic phosphate esters such as OMFP or FDP. Such assays therefore suffer from unreliability due to detection of spurious phosphate group hydrolysis by contaminating phosphatases that are not PTPs, and/or inefficient hydrolysis by PTPs of the artificial organic phosphate ester substrates.

20 Another type of PTP assay employs substrates for which PTPs have high specificity, such as tyrosine phosphorylated proteins or peptides. These assays detect PTP activity by monitoring the release of free phosphate following PTP hydrolysis of such substrates. These assays are time-consuming and expensive, and involve additional procedural measures related to the storage, handling and disposal of radioactive materials.

25 Clearly a need exists for improved reagents and assays for identifying agents that modulate dephosphorylation processes. The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

In one aspect, the present invention provides an isolated polypeptide comprising the amino acid sequence $-C(X)_5-R-$ (SEQ ID NO:1), wherein C is cysteine, R is arginine, and X is any amino acid residue, and wherein a sulfur atom of the cysteine is covalently linked to a main-chain nitrogen atom of an adjacent C-terminal amino acid residue; an isolated protein tyrosine phosphatase polypeptide in a cyclic sulfenyl-amide form (PTP-SN); and an isolated polypeptide comprising the sequence $-Cys(X)_5-Arg-$ (SEQ ID NO:1), wherein X is any amino acid residue, and wherein the cysteine residue and the adjacent C-terminal amino acid residue in SEQ ID NO:1 form the following chemical structure



wherein R is the amino acid side chain of the adjacent C-terminal amino acid residue. In certain embodiments, the polypeptide is PTP1B comprising the amino acid sequence set forth in any one of SEQ ID NOS:24, 26, and 30; cdc14a comprising the amino acid sequence set forth in any one of SEQ ID NOS:85, 87, and 89; cdc14b comprising the amino acid sequence set forth in any one of SEQ ID NOS:91 and 93; cdc25a comprising the amino acid sequence set forth in any one of SEQ ID NOS:67 and 69; cdc25b comprising the amino acid sequence set forth in any one of SEQ ID NOS:77 and 79; cdc25c comprising the amino acid sequence set forth in any one of SEQ ID NOS:81 and 83; DSP-3/JSP-1 comprising the amino acid sequence set forth in SEQ ID NO:97; or DEP-1 comprising the amino acid sequence set forth in any one of SEQ ID NOS:38 and 40.

In another embodiment, the invention provides an isolated protein tyrosine phosphatase (PTP) enzyme comprising a sequence $[I/V]HCXAGXXR[S/T]G$ (SEQ ID NO:106), wherein X is any amino acid, and wherein cysteine in SEQ ID NO:106 and the

adjacent C-terminal residue together form a cyclic sulfenyl-amide group between the sulfur atom of the cysteine and the main-chain nitrogen atom of the adjacent C-terminal residue. In particular embodiments, the PTP is (a) PTP1B comprising the amino acid sequence set forth in any one of SEQ ID NOS:24, 26, and 30 or (b) DEP-1 comprising the amino acid sequence set forth in any one of SEQ ID NOS:38 and 40.

The invention also provides a method of making a protein tyrosine phosphatase in a cyclic sulfenyl-amide form (PTP-SN) comprising subjecting a biological sample comprising a PTP that comprises the sequence C-(X)₅-R (SEQ ID NO:1), wherein X is any amino acid, to oxidation conditions for a time and under conditions sufficient to induce the cysteine residue of SEQ ID NO:1 to form a cyclic sulfenyl-amide with the adjacent C-terminal residue.

Also provided by the present invention is a method for identifying a compound that hinders reduction of a cyclic sulfenyl-amide protein tyrosine phosphatase (PTP-SN) comprising (a) introducing a PTP-SN to a test compound to form a composition; (b) adding a reducing agent to the composition of (a) under conditions and for a time sufficient to permit binding of the test compound to the PTP-SN; and (c) analyzing the composition to determine the presence or absence of PTP-SN. In certain embodiments, the reducing agent is beta-mercaptoethanol, dithiothreitol (DTT), dithioerythritol (DTE), glutathione, or a phosphine. In another embodiment, the step of analyzing comprises performing a functional assay on the composition to determine PTP catalytic activity. In a particular embodiment, the compound stabilizes the PTP-SN in the oxidized state. In one embodiment, the PTP is PTP1B comprising the amino acid sequence set forth in any one of SEQ ID NOS:24, 26, and 30; cdc14a comprising the amino acid sequence set forth in any one of SEQ ID NOS:85, 87, and 89; cdc14b comprising the amino acid sequence set forth in any one of SEQ ID NOS:91 and 93; cdc25a comprising the amino acid sequence set forth in any one of SEQ ID NOS:67 and 69; cdc25b comprising the amino acid sequence set forth in any one of SEQ ID NOS:77 and 79; cdc25c comprising the amino acid sequence set forth in any one of SEQ ID NOS:81 and 83; DSP-3/JSP-1 comprising the

amino acid sequence set forth in SEQ ID NO:97; or DEP-1 comprising the amino acid sequence set forth in any one of SEQ ID NOS:38 and 40.

In another embodiment, the invention provides a method for identifying a compound that binds to a protein tyrosine phosphatase sulfenyl-amide form (PTP-SN) comprising (a) contacting a PTP-SN with a test compound; and (b) determining binding of the compound to the PTP-SN, thereby identifying a compound that binds to the PTP-SN. In certain embodiments, the compound does not bind to a PTP-SN that has been converted to a catalytically active PTP by reducing conditions. In a particular embodiment, the step of determining binding comprises performing X-ray crystallographic analysis. In another particular embodiment, the compound stabilizes the PTP-SN in the oxidized state. In one embodiment, the PTP is PTP1B comprising the amino acid sequence set forth in any one of SEQ ID NOS:24, 26, and 30; cdc14a comprising the amino acid sequence set forth in any one of SEQ ID NOS:85, 87, and 89; cdc14b comprising the amino acid sequence set forth in any one of SEQ ID NOS:91 and 93; cdc25a comprising the amino acid sequence set forth in any one of SEQ ID NOS:67 and 69; cdc25b comprising the amino acid sequence set forth in any one of SEQ ID NOS:77 and 79; cdc25c comprising the amino acid sequence set forth in any one of SEQ ID NOS:81 and 83; DSP-3/JSP-1 comprising the amino acid sequence set forth in SEQ ID NO:97; or DEP-1 comprising the amino acid sequence set forth in any one of SEQ ID NOS:38 and 40.

In another embodiment, a method is provided for identifying a compound that modulates or hinders reduction of a cyclic sulfenyl-amide protein tyrosine phosphatase-1B (PTP1B-SN) comprising: (a) obtaining crystalline PTP1B-SN; (b) introducing a test compound to the crystalline PTP1B-SN under conditions and for a time sufficient to permit binding of the test compound to the PTP1B-SN; and (c) analyzing the crystalline PTP1B-SN to determine whether the test compound binds thereto. In another specific embodiment, the invention provides a method for identifying a compound that hinders reduction of a cyclic sulfenyl-amide protein tyrosine phosphatase-1B (PTP1B-SN) comprising: (a) introducing a test compound to the PTP1B-SN to form a composition; (b) adding a reducing agent to the composition of (a), under conditions and for a time sufficient to

permit binding of the test compound to the PTP1B-SN; and analyzing the composition to determine the presence or absence of PTP1B-SN.

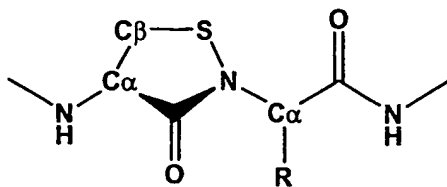
The invention also provides a double mutant protein tyrosine phosphatase (PTP) polypeptide having the amino acid sequence -CS(X)₄-R- set forth in SEQ ID NO:109, wherein X is any amino acid, said mutant PTP comprising a substitution of the cysteine in SEQ ID NO:1 and a substitution of the amino acid that is the adjacent C-terminal residue to the cysteine residue. In a particular embodiment, the catalytic domain of the double mutant PTP possesses a three-dimensional structure that is substantially similar to the three-dimensional structure of the catalytic domain of the corresponding PTP-SN. In certain embodiments, the cysteine residue is substituted with an alanine residue and/or the adjacent C-terminal residue is substituted with an alanine residue.

In another embodiment, the invention provides a double mutant protein tyrosine phosphatase (PTP) polypeptide having the amino acid sequence -H-C-S-X-G-X-G-R-X-G- set forth in SEQ ID NO:21, wherein X is any amino acid, and the mutant PTP comprises (a) a substitution of the cysteine in SEQ ID NO:21, and (b) a substitution of the serine that is adjacent to the cysteine residue. In a particular embodiment, the catalytic domain of the double mutant PTP possesses a three-dimensional structure that is substantially similar to the three-dimensional structure of the catalytic domain of the corresponding PTP-SN.. In certain particular embodiments, the double mutant PTP polypeptide is PTP1B comprising the amino acid sequence set forth in any one of SEQ ID NOS:24, 26, and 30 or DEP-1 comprising the amino acid sequence set forth in any one of SEQ ID NO:38 and 40.

The invention also provides a double mutant protein tyrosine phosphatase-1B (PTP1B) polypeptide comprising the amino acid sequence of SEQ ID NO:109 in which the cysteine in SEQ ID NO:109 is substituted and the serine in SEQ ID NO:109 is substituted, wherein the cysteine is located at position number 215 in any one of SEQ ID NOS:24, 26, and 30 and the serine is located at position number 216 in any one of SEQ ID NOS:24, 26, and 30, and wherein the double mutant PTP1B is at least 80% identical, at least 90% identical, at least 95% identical, or at least 99% identical to the amino acid

sequence set forth in any one of SEQ ID NOS:24, 26, and 30. In a particular embodiment, the cysteine located at position 215 is substituted with an alanine residue, and the serine located at position 216 is substituted with an alanine residue. In another particular embodiment, the double mutant PTP comprises the amino acid sequence set forth
5 in SEQ ID NO:110.

In another embodiment, the invention provides an antibody, or an antigen-binding fragment thereof, that binds to at least one polypeptide selected from (a) a double mutant protein tyrosine phosphatase (PTP) polypeptide having the amino acid sequence –CS(X)₄-R- set forth in SEQ ID NO:109, wherein X is any amino acid, and wherein the
10 mutant PTP comprises a substitution of the cysteine in SEQ ID NO:1 and a substitution of an amino acid that is an adjacent C-terminal residue to the cysteine residue; wherein the catalytic domain of the double mutant PTP possesses a three-dimensional structure that is substantially similar to the three-dimensional structure of the catalytic domain of the corresponding PTP-SN; (b) a double mutant protein tyrosine phosphatase (PTP)
15 polypeptide having the amino acid sequence -H-C-S-X-G-X-G-R-X-G- set forth in SEQ ID NO:21, wherein X is any amino acid, and wherein the mutant PTP comprises (1) a substitution of the cysteine in SEQ ID NO:21, and (2) a substitution of serine that is adjacent to the cysteine residue; wherein the catalytic domain of the double mutant PTP possesses a three-dimensional structure that is substantially similar to the three-dimensional
20 structure of the catalytic domain of the corresponding PTP-SN; (c) a PTP-SN polypeptide comprising comprising the amino acid sequence –C(X)₅-R- (SEQ ID NO:1), wherein C is cysteine, R is arginine, and X is any amino acid residue, and wherein a sulfur atom of the cysteine is covalently linked to a main-chain nitrogen atom of an adjacent C-terminal amino acid residue; or (d) a PTP-SN polypeptide comprising the sequence Cys-(X)₅-Arg
25 (SEQ ID NO:1), wherein X is any amino acid residue, and wherein the cysteine residue and an adjacent C-terminal amino acid residue in SEQ ID NO:1 form the following chemical structure



wherein R is the amino acid side chain of the adjacent C-terminal amino acid residue. In another embodiment, the antibody or antigen binding fragment thereof binds to at least two polypeptides. In another particular embodiment, the antibody or antigen binding fragment thereof binds to at least one double mutant PTP polypeptide and to at least one PTP-SN polypeptide. In certain embodiments the antibody is a polyclonal antibody or a monoclonal antibody. The monoclonal antibody is a mouse monoclonal antibody, a human monoclonal antibody, a rat monoclonal antibody, or a hamster monoclonal antibody. In another embodiment, the antigen-binding fragment is a Fab, a Fab', a F(ab')₂, a Fv, or a Fd fragment. The antibody may be a chimeric antibody, a humanized antibody, or a single chain antibody. The invention also provides a hybridoma that produces the monoclonal antibody and also provides a host cell that expresses an antibody or an antigen-binding fragment thereof. In another embodiment, the invention provides such antibody or antibody fragment and a physiological carrier.

15 In another embodiment, the invention provides a method for identifying an agent that binds specifically to a double mutant protein tyrosine phosphatase (PTP) polypeptide comprising (a) contacting a double mutant PTP as described herein (having the amino acid sequence -CS(X)₄-R- set forth in SEQ ID NO:109, wherein X is any amino acid, said mutant PTP comprising a substitution of the cysteine in SEQ ID NO:1 and a
20 substitution of the amino acid that is the adjacent C-terminal residue to the cysteine residue or a double mutant protein tyrosine phosphatase (PTP) polypeptide having the amino acid sequence -H-C-S-X-G-X-G-R-X-G- set forth in SEQ ID NO:21, wherein X is any amino acid, and the mutant PTP comprises a substitution of the cysteine in SEQ ID NO:21 and a substitution of the serine that is adjacent to the cysteine residue) with a candidate agent
25 under conditions and for a time sufficient to permit interaction between the mutant PTP and the candidate agent; (b) contacting the corresponding wildtype PTP polypeptide with the

candidate agent under conditions and for a time sufficient to permit interaction between the wildtype PTP and the candidate agent; (c) comparing the level of binding of the candidate agent to the mutant PTP with the level of binding of the candidate agent to the wildtype PTP, wherein an increased level of binding to the mutant PTP relative to the level of binding to the wildtype PTP indicates that the agent specifically binds to the mutant PTP polypeptide.

In another embodiment, a method is provided for identifying an agent that alters reduction of a protein tyrosine phosphatase sulfenyl-amide form (PTP-SN) comprising: (a) contacting a double mutant PTP polypeptide as described herein with a candidate agent under conditions and for a time sufficient to permit interaction between the mutant PTP and the candidate agent; (b) contacting the corresponding wildtype PTP polypeptide with the candidate agent under conditions and for a time sufficient to permit interaction between the wildtype PTP and the candidate agent; (c) determining a level of binding of the candidate agent to the mutant PTP; (d) determining a level of binding of the candidate agent to the wildtype PTP; and (e) comparing the level of binding of the candidate agent to the mutant PTP relative to the level of binding of the candidate agent to the wildtype PTP, wherein an increased or decreased level of binding of the candidate agent to the mutant PTP indicates that the agent alters reduction of a PTP-SN. The double mutant PTP has the amino acid sequence -CS(X)₄-R- set forth in SEQ ID NO:109, wherein X is any amino acid, and wherein the mutant PTP comprises a substitution of the cysteine in SEQ ID NO:1 and a substitution of the amino acid that is the adjacent C-terminal residue to the cysteine residue. In another embodiment, the double mutant protein tyrosine phosphatase (PTP) polypeptide having the amino acid sequence -H-C-S-X-G-X-G-R-X-G- set forth in SEQ ID NO:21, wherein X is any amino acid, and the mutant PTP comprises a substitution of the cysteine in SEQ ID NO:21 and a substitution of the serine that is adjacent to the cysteine residue.

These and other aspects of the invention will become evident upon reference to the following detailed description and attached drawings. In addition,

various references to published documents are set forth herein which describe in more detail certain aspects of this invention, and are therefore incorporated by reference in their entireties.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

5 Figure 1 presents electron density maps showing that the oxidation of PTP1B resulted in formation of a sulfenyl-amide bond between the thiol Cys215 and the amide nitrogen of Ser216. Figure 1A is a stereo view of the electron density map of the PTP loop in the sulfenyl-amide structure, which was calculated using $2Fo-Fc$, $Fo-Fc$, and $-|Fo-Fc|$ Fourier coefficients. The closed arrowhead and open arrowhead correspond to
10 electron densities calculated using $Fo-Fc$, and $-|Fo-Fc|$ Fourier coefficients, respectively. The $Fo-Fc$ electron density indicated that no oxygen atoms were attached to the Cys215 sulfur atom, but that a small amount of the enzyme was still reduced. Figure 1B presents electron density maps ($2Fo-Fc$) showing the time-dependent changes at the catalytic Cys215 of PTP1B by oxidation for six time points over a 16-hour period. At 40 and 75
15 minutes a mixture of reduced and oxidized (sulfenyl-amide) states were present. In Figure 1B, (red) = reduced state; (red+ox) = reduced plus oxidized states; (ox) = oxidized state; (SO_2/SO_3) = mixture of sulfinic and sulfonic acid states. Figures were drawn using PYMOL (*see* Internet:<http://pymol.sourceforge.net/>).

 Figure 2 shows the conformational changes accompanying oxidation of
20 PTP1B. Figure 2A presents a ribbons diagram showing the catalytic site of reduced PTP1B. Figure 2B shows the sulfenyl-amide species of PTP1B in the same orientation as reduced PTP1B in Figure 2A. Figure 2C illustrates superimposition of reduced and sulfenyl-amide states of PTP1B. The view has been rotated relative to the diagrams presented in Figure 2A and 2B for clarity. In the figure, "(red)" = reduced and "(ox)" =
25 oxidized. Figures were drawn using PYMOL (*see* Internet:<http://pymol.sourceforge.net/>). Figure 2D illustrates the chemical mechanism for generation of the sulfenyl-amide bond. "X:" denotes a nucleophile.

Figure 3 shows a pulse-chase analysis of oxidation of PTP1B in solution. Figure 3A represents SDS-PAGE gels of wild-type PTP1B (top left) and the substrate trapping mutant C215S PTP1B (top right) incubated with increasing concentrations of H_2O_2 and the corresponding MALDI mass spectra for the Cys215- and Ser216-containing peptides after trypsinolysis (bottom panel). At high concentrations of $\text{H}_2^{16}\text{O}_2$ (10^3 and 10^4 μM), irreversible oxidation was accompanied by a shift in the mass of the active site peptide of 32 and 48 dalton (Da) (corresponding to the addition of two or three oxygens). Irreversible oxidation was also accompanied by retardation in electrophoretic mobility of the protein observed on SDS PAGE. No change in molecular weight (M_r) was observed for the equivalent peptide from the PTP1B-C215S control at any concentration of H_2O_2 tested (right). Figure 3B shows inhibition of PTP1B catalytic activity by $\text{H}_2^{18}\text{O}_2$. Enzymatically active PTP1B was incubated with increasing amounts of $\text{H}_2^{18}\text{O}_2$ for 30 minutes at room temperature and then divided into 3 aliquots. One aliquot was assayed for enzyme activity, and another was assayed for reversibility of oxidation. A third aliquot was incubated for 2 hours with greater than 100-fold excess of $\text{H}_2^{16}\text{O}_2$. The molecular weights of the tryptic digest active site peptides were determined. For each concentration of H_2O_2 , activity is shown in the left panel and the equivalent MALDI mass spectrum is shown on the right. At concentrations of $\text{H}_2^{18}\text{O}_2$ up to 320 μM , inhibition of enzyme activity was reversible with approximately 90% of enzyme activity recovered upon reactivation. At high concentrations of $\text{H}_2^{18}\text{O}_2$ or $\text{H}_2^{16}\text{O}_2$ (50 mM), oxidation and inactivation were irreversible and yielded the sulfonic acid (Cys- SO_3) derivative with an increase in peptide mass of +54 and +48 Da, respectively. Under conditions of reversible oxidation in the presence of $\text{H}_2^{18}\text{O}_2$, which would not oxidize the Cys residue beyond the sulfenic acid (Cys-SO) form, followed by a chase with excess $\text{H}_2^{16}\text{O}_2$, the sulfonic acid derivative produced displayed an increased mass of +48 (3 atoms of ^{16}O). No sulfonic acid derivative was detected that displayed an increase in mass of +50 (1 atom of ^{18}O and 2 atoms of ^{16}O) although the mass resolution of the technique (± 0.3 Da) was sufficient for its detection.

Figure 4 illustrates the effects of oxidation on substrate binding and phosphorylation of PTP1B. Figure 4A illustrates the inter-relationship of PTP1B redox species. The reaction mechanism presented shows that in response to H_2O_2 , Cys215 is oxidized to sulfenic acid and activity is inhibited. Rapid reaction of sulfenic acid with the amide of Ser216 eliminates water, generating the sulfenyl-amide species, which by reacting with thiols generates mixed disulfide intermediates and reduction of the enzyme, returning it to an active state. In a competing reaction, sulfenic acid is oxidized to the irreversible sulfinic and sulfonic acids in a process that could be accelerated by high concentrations of H_2O_2 and strong oxidizing agents, *e.g.*, pervanadate. Figure 4B: Examination of the effects of oxidation on binding of the insulin receptor kinase (IRK) by a substrate trapping mutant form of PTP1B (D181A PTP1B). PTP1B was immunoprecipitated with antibody FG6, and the PTP1B immunoprecipitates were immunoblotted with anti-pTyr antibodies (upper panel) and an anti-IRK antibody (middle panel), which revealed that increasing concentrations of H_2O_2 led to disruption of a PTP1B/IR complex, and that tyrosyl phosphorylation of PTP1B by the IRK was enhanced at higher concentrations of H_2O_2 . Ponceau S staining of the filter confirmed that an equal amount of PTP1B was immunoprecipitated from each sample (lower panel). Figure 4C: Mutation of Tyr46 in PTP1B led to attenuation of oxidation induced phosphorylation of the PTP by the insulin receptor kinase. Tyrosyl phosphorylation of PTP mutants PTP1B D181A and PTP1B D181A/Y46F in the IR kinase assay described above, are compared in the autoradiograph (48 hour exposure, upper panel). The lower panel shows the Coomassie blue stained gel.

Figure 5 shows the structural relationships between cysteine thiol, cysteine sulfenic acid, and cysteine sulfenyl amide.

Figure 6 presents the sequence alignment of classical PTPs with the signature motif -C-(X)₅-R- (SEQ ID NO:1), which is illustrated at the bottom.

Figure 7 shows the sequence alignment of dual specificity phosphatases with the signature motif -C-(X)₅-R- illustrated at the bottom.

Figure 8 shows the sulfenyl-amide species reduced to SH using either DTT or glutathione. Figure 8(A) presents the electron density map of Cys215 in the sulfenyl-amide state before reduction. Figure 8(B) illustrates the electron density map after incubation with DTT, and Figure 8(C) shows the electron density map after reduction by glutathione, in which the SH state was recovered. The sulfenyl-amide species eventually oxidized to the irreversible Cys-SO₃ state after 3 months as illustrated in Figure 8(D), which was identical in conformation to pervanadate-induced oxidation of PTP1B, shown as a stereoview in Figure 8(E).

Figure 9 shows the Nano-flow electrospray spectra of reduced PTP1B, Mr 37310.74±0.24 Da (Figure 9A) and oxidized PTP1B, Mr 37309.2±0.18 Da (Figure 9B). A mass difference of 1.5 Da was observed. The theoretical mass of the PTP1B construct is 37312.6 Da. On formation of the sulfenyl-amide species a loss of 2 Da (loss of protons from -SH of Cys 215 and NH of Ser 216 (uncharged PTP1B)) was expected.

DETAILED DESCRIPTION OF THE INVENTION

The invention relates to the surprising discovery that when a protein tyrosine phosphatase (PTP) is oxidized, a sulfenic acid intermediate is produced and is rapidly converted into a previously unknown form, namely a sulfenyl-amide species, wherein the sulfur atom of the catalytic cysteine is covalently linked to the polypeptide backbone nitrogen atom of the amino acid residue situated immediately C-terminal to the cysteine, thus creating a cyclic sulfenyl-amide form. Oxidation of PTP to the cyclic sulfenyl-amide form is also accompanied by significant, or large, conformational changes in the catalytic site that effectively inhibit substrate binding. This unusual protein modification protects the active site cysteine residue of a PTP from irreversible oxidation to sulfinic acid and sulfonic acid and permits redox regulation of the enzyme by promoting its reversible reduction by thiols. As described herein, compositions and methods related to these discoveries may find a variety of uses, for instance, in drug screening (including antibody screening) and therapeutic applications whereby at least

one functionally compromised PTP-sulfenyl amide (PTP-SN) is stabilized in the sulfenyl amide form, thereby reducing the level of active PTP.

In addition, it has been discovered that the sulfur atom of the PTP catalytic cysteine can form a disulfide bond ("SS") with the sulfur atom of a conformationally-proximal or nearby cysteine residue. Such a disulfide bond effectively inactivates the PTP until such PTP-SS is exposed to appropriate reducing conditions, whereupon it may be reactivated. Such PTPs herein are designated as "PTP-SS" polypeptides (*see, e.g.,* Caselli et al., *J. Biol. Chem.* 273:32554-60 (1998); Chiarugi et al., *J. Biol. Chem.* 276:33478-87 (2001); Fauman et al., *Cell* 93: 617-625 (1998); Reynolds et al., *J. Mol. Biol.* 293: 559-568 (1999); Savitsky et al., *J. Biol. Chem.* 277: 20535-20540 (2002); Hanlon et al., *Protein Sci.* 7: 508-511 (1998); Song et al., *Mol. Cell* 7:615-626 (2001); Lee et al., *J. Biol. Chem.* 277: 20336-20342 (2002)).

In certain embodiments, the invention is directed to compositions and methods for monitoring and regulating PTP activity, including methods for identifying agents or compounds that inhibit, regulate, modulate, or alter (*e.g.,* increase or decrease with statistical significance), and preferably that decrease, the activity of a native PTP. Such compositions comprise novel, oxidized forms of PTPs, or mutated PTPs described herein below that structurally mimic, or act as a surrogate for, such oxidized PTPs. The methods described herein comprise assays useful for identifying compounds that can modulate, regulate, hinder, inhibit, or otherwise alter the reduction of the inactivated oxidized sulfenyl-amide form of the PTP. In certain preferred embodiments, agents identified by these assays are antagonists of PTP activity (*e.g.,* agents that inhibit, hinder, or decrease the activity of the PTP). The agent may be an endogenous physiological substance or may be an antibody or a natural or synthetic drug, including an organic small molecule as provided herein.

As used herein, the term "PTP" means a protein tyrosine phosphatase enzyme capable of dephosphorylating a phosphorylated tyrosine residue in a protein, polypeptide, or peptide. Such PTPs of the invention are identified by their signature catalytic cysteine motif: -C-(X)₅-R- (SEQ ID NO:1), wherein the cysteine residue is the

catalytic cysteine and wherein "X" can be any amino acid residue, natural or unnatural. The definition of PTP herein includes "classical" PTPs, which dephosphorylate tyrosine residues, and which have the signature motif sequence -C-S-X₄-R- (SEQ ID NO:109), for example, -H-C-S-X-G-X-G-R-X-G- (SEQ ID NO:21), wherein "X" can be any amino acid residue. Andersen et al. (*Mol. Cell. Bio.* 21:7117-7136 (2001); *FASEB J.* 18:8-30 (2004), which as also noted above are incorporated herein by reference) describe and illustrate this structural relationship among classical protein tyrosine phosphatase domains. Such classical PTPs are described, and GenBank reference numbers provided therefor, in Andersen et al. (2001 *Mol. Cell. Biol.* 21:7117) and herein.

For example, the PTP may be PTP1B (*e.g.*, GenBank Accession Nos. M31724 (SEQ ID NOS:23-24); NM_002827 (SEQ ID NOS:25-26); NM_011201 (SEQ ID NOS:27-28); M33689 (SEQ ID NOS:29-30); M33962 (SEQ ID NOS:31-32)); PTP-epsilon (*e.g.*, Genbank Accession Nos. NM_006504 (SEQ ID NOS:33-34) and NM_130435 (SEQ ID NOS:35-36)); DEP-1 (CD148; PTP-eta; F-36-12) (U10886 (SEQ ID NOS:37-38); D37781 (SEQ ID NOS:39-40); AAB26475 (SEQ ID NO:41); U.S. Patent No. 6,114,140); and SEQ ID NO:159-160)); TCPTP (*e.g.*, GenBank Accession Nos. M25393 (SEQ ID NOS:163-164); NM_002828 (SEQ ID NOS:165-166); NM_080422 (SEQ ID NOS:167-168); PTPH1 (SEQ ID NO:96-97; U.S. Patent Nos. 5,595,911; 5,863,781; 6,479,640); SHP2 (*e.g.*, GenBank Accession Nos. D13540 (SEQ ID NOS:42-43); L03535 (SEQ ID NOS:44-45); L07527 (SEQ ID NOS: 46-47); X70766 (SEQ ID NOS: 48-49); L08807 (SEQ ID NO: 50); S78088 (SEQ ID NOS: 51-52); S39383 (SEQ ID NO: 53); D84372 (SEQ ID NOS: 54-55); U09307 (SEQ ID NOS: 56-57)); SHP1 (M74903 (SEQ ID NOS: 58-59); X62055 (SEQ ID NOS: 60-61); M77273 (SEQ ID NOS: 62-63); M90388 (SEQ ID NOS: 64-65); cdc25a (*e.g.*, GenBank Accession Nos. NM_001789 (SEQ ID NOS: 66-67), AF527417 (SEQ ID NOS: 68-69), NM_133571 (SEQ ID NOS: 70-71)); cdc25b (*e.g.*, GenBank Accession Nos. NM_133572 (SEQ ID NOS: 72-73), NM_023117 (SEQ ID NOS: 74-75), NM_021872 (SEQ ID NOS: 76-77); M81934 (SEQ ID NOS: 78-79); cdc25c (*e.g.*, GenBank Accession Nos. NM_001790 (SEQ ID NOS: 80-81), NM_022809 (SEQ ID NOS: 82-

83)); cdc14a (e.g., GenBank Accession Nos. AF122013 (SEQ ID NOS: 84-85); AF064102 (SEQ ID NOS: 86-87); AF064103 (SEQ ID NOS: 88-89); Li et al., 1997 *J. Biol. Chem.* 272:29403; U.S. Patent No. 6,331,614); cdc14b (e.g., GenBank Accession Nos. AF064104 (SEQ ID NOS: 90-91); AF064105 (SEQ ID NOS: 92-93)); DSP-2 (WO 00/56899) (SEQ ID NOS: 94-95); DSP-3 (WO 00/60092) (SEQ ID NOS: 96-97); DSP-4 (U.S. Patent Publication No. 2003/175829; (SEQ ID NOS: 112-113)); DSP-5 (SEQ ID NOS: 114-115; DSP-5 alternate form (SEQ ID NOS: 116-117); U.S. Patent Application No. 6,645,753;); DSP-6; DSP-7 (WO 00/60098); (SEQ ID NOS: 118-120)); DSP-8 (WO 00/63393; (SEQ ID NOS: 121-122)); DSP-9 (U.S. Patent No. 6,492,157; (SEQ ID NOS: 123-124)); DSP-10 (U.S. Patent No. 6,551,810; (SEQ ID NOS: 125-126)); DSP-11 (U.S. Patent No. 6,649,391; WO 01/05983; (SEQ ID NOS: 127-128)); DSP-12 (U.S. Patent Publication No. 2001/049358; U.S.A.N. 09/775,925; (SEQ ID NOS: 129-130)); DSP-13 (U.S. Patent Publication No. 2001/049358; U.S.A.N. 09/775,925; (SEQ ID NOS: 131-132)); DSP-14 (U.S.A.N. 09/847,519 and WO 01/46394; (SEQ ID NOS: 133-134)); DSP-15 (SEQ ID NOS: 135-136; DSP-15 alternate form (SEQ ID NOS: 137-138); U.S. Patent Publication No. 2002/182203); DSP-16 (SEQ ID NOS: 139-140; DSP-16 alternate form (SEQ ID NOS: 141-142); U.S. Patent Publication No. 2002/137170); DSP-17 (U.S.A.N. 10/076,859; (SEQ ID NOS: 143-144)); DSP-18 (U.S. Patent Publication No. 2003/092114; (SEQ ID NOS: 145-158)); CD45 (Charbonneau et al., *Proc. Natl. Acad. Sci. USA* 85:7182-86 (1988); Genbank Accession Nos. NM_080922 (SEQ ID NOS: 98-99), NM_080921 (SEQ ID NOS: 100-101), NM_002838 (SEQ ID NOS: 102-103), and NM_080923) (SEQ ID NOS: 104-105). Conserved amino acids may be readily found at positions in a PTP polypeptide, particularly within the signature catalytic cysteine motif and at positions proximal to the motif, toward both the amino terminus and toward the carboxy terminus of the PTP and flanking the signature motif (for example, [I/V]HCXAGXXR[S/T]G (SEQ ID NO:106). In addition to comprising the motif sequence of SEQ ID NO:1, PTPs of the invention may comprise any of the following sequences:

	His-Cys-(X) ₅ -Arg	(SEQ ID NO:2)
	Val-His-Cys-(X) ₅ -Arg	(SEQ ID NO:3)
	Ile-His-Cys-(X) ₅ -Arg	(SEQ ID NO:4)
	Cys-(X) ₅ -Arg-Ser	(SEQ ID NO:5)
5	Cys-(X) ₅ -Arg-Thr	(SEQ ID NO:6)
	Cys-(X) ₅ -Arg-Ser-Gly	(SEQ ID NO:7)
	Cys-(X) ₅ -Arg-Thr-Gly	(SEQ ID NO:8)
	His-Cys-(X) ₅ -Arg-Ser	(SEQ ID NO:9)
	His-Cys-(X) ₅ -Arg-Thr	(SEQ ID NO:10)
10	His-Cys-(X) ₅ -Arg-Ser-Gly	(SEQ ID NO:11)
	His-Cys-(X) ₅ -Arg-Thr-Gly	(SEQ ID NO:12)
	Val-His-Cys-(X) ₅ -Arg-Ser	(SEQ ID NO:13)
	Val-His-Cys-(X) ₅ -Arg-Ser-Gly	(SEQ ID NO:14)
	Val-His-Cys-(X) ₅ -Arg-Thr	(SEQ ID NO:15)
15	Val-His-Cys-(X) ₅ -Arg-Thr-Gly	(SEQ ID NO:16)
	Ile-His-Cys-(X) ₅ -Arg-Ser	(SEQ ID NO:17)
	Ile-His-Cys-(X) ₅ -Arg-Ser-Gly	(SEQ ID NO:18)
	Ile-His-Cys-(X) ₅ -Arg-Thr	(SEQ ID NO:19)
	Ile-His-Cys-(X) ₅ -Arg-Thr-Gly	(SEQ ID NO:20)
20		

wherein X can be any amino acid residue, natural or unnatural. PTPs include PTP1B and PTPs comprising the sequences as listed in Figure 6, and those PTPs known in the art as well as naturally-occurring splice-variants or mutants thereof, provided that such PTPs comprise the sequence of SEQ ID NO:1. PTPs also include dual specificity phosphatases, also known as DSPs. A DSP is a dual specificity phosphatase enzyme that can dephosphorylate a phosphorylated Tyr residue as well as phosphorylated Ser or Thr residues of proteins. Exemplary DSPs are listed in Figure 7 herein. Figure 7 also provides a sequence alignment of catalytic domain regions of DSP polypeptides. The DSPs also comprise the signature catalytic cysteine motif set forth in SEQ ID NO:1.

Further included in the definition of a PTP are variant or mutant polypeptides having at least 70%, 80%, 85%, 90%, 95%, 98%, or 99% identity to a sequence in Figure 6 or Figure 7 or to a sequence of any other PTP known in the art, provided that such variant or mutant polypeptides comprise a sequence of amino acids selected from any of the sequences set forth in SEQ ID NOS: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 106, 107, and 109. Such a PTP variant has a polypeptide sequence at least 70%, 80%, 85%, 90%, 95%, 98%, or 99% identity to a sequence of a full-length PTP disclosed herein or known in the art.

The term "PTP-SN" means a PTP, such as a classical PTP and/or a DSP, or a variant thereof (also termed herein as a cyclic sulfenylamide, hence the abbreviated term "PTP-SN"), as described herein, wherein the sulfur atom of the catalytic cysteine is covalently bonded to the main-chain nitrogen atom of the adjacent C-terminal residue. The main-chain nitrogen of an amino acid, as is well understood in the art, is the nitrogen that contributes to the formation of the peptide bond that forms the backbone of a peptide or polypeptide. A peptide bond is formed by elimination of water from the carboxyl group of one amino acid and the α -amino group of the next or adjacent amino acid, which is the amino acid that is situated toward the carboxy terminus of the polypeptide, that is, the adjacent C-terminal residue. A PTP that may form a PTP-SN can be any one of those known in the art as well as a naturally-occurring splice-variant or mutant that has a sequence selected from any of the sequences set forth in SEQ ID NOS: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 21; or a sequence disclosed in Andersen et al. (2001 *Mol. Cell. Biol.* 21:7117; 2004 *FASEB J.* 18:8). The PTP-SN may also be formed from a PTP polypeptide variant that has at least 70%, 80%, 85%, 90%, 95%, 98%, or 99% sequence identity to a sequence shown or described in Figure 6 herein, Figure 7 herein, or disclosed in Andersen et al. (*supra*, 2001; 2004), provided such PTP-SN or PTP-SN polypeptide variant comprises a sequence set forth in SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 106, 107, and 109; wherein the sulfur atom of the catalytic cysteine is covalently bonded to the main-chain nitrogen atom of the adjacent C-terminal residue.

While all PTP-SN molecules comprise the signature catalytic cysteine motif sequence of SEQ ID NO:1, PTP-SNs may comprise any of the motif sequences selected from:

	His-Cys-(X) ₅ -Arg	(SEQ ID NO:2)
5	Val-His-Cys-(X) ₅ -Arg	(SEQ ID NO:3)
	Ile-His-Cys-(X) ₅ -Arg	(SEQ ID NO:4)
	Cys-(X) ₅ -Arg-Ser	(SEQ ID NO:5)
	Cys-(X) ₅ -Arg-Thr	(SEQ ID NO:6)
	Cys-(X) ₅ -Arg-Ser-Gly	(SEQ ID NO:7)
10	Cys-(X) ₅ -Arg-Thr-Gly	(SEQ ID NO:8)
	His-Cys-(X) ₅ -Arg-Ser	(SEQ ID NO:9)
	His-Cys-(X) ₅ -Arg-Thr	(SEQ ID NO:10)
	His-Cys-(X) ₅ -Arg-Ser-Gly	(SEQ ID NO:11)
	His-Cys-(X) ₅ -Arg-Thr-Gly	(SEQ ID NO:12)
15	Val-His-Cys-(X) ₅ -Arg-Ser	(SEQ ID NO:13)
	Val-His-Cys-(X) ₅ -Arg-Ser-Gly	(SEQ ID NO:14)
	Val-His-Cys-(X) ₅ -Arg-Thr	(SEQ ID NO:15)
	Val-His-Cys-(X) ₅ -Arg-Thr-Gly	(SEQ ID NO:16)
	Ile-His-Cys-(X) ₅ -Arg-Ser	(SEQ ID NO:17)
20	Ile-His-Cys-(X) ₅ -Arg-Ser-Gly	(SEQ ID NO:18)
	Ile-His-Cys-(X) ₅ -Arg-Thr	(SEQ ID NO:19)
	Ile-His-Cys-(X) ₅ -Arg-Thr-Gly	(SEQ ID NO:20)
	[I/V]HCXAGXXR[S/T]G	(SEQ ID NO:106)
	C(X) ₅ -R[S/T]	(SEQ ID NO:107)
25	and CS-(X) ₄ -R	(SEQ ID NO:109);

wherein X is any amino acid residue, natural or unnatural, wherein the sulfur atom of the catalytic cysteine is covalently bonded to the main-chain nitrogen atom of the adjacent C-terminal residue. The PTP polypeptide that is not in the SN form described herein but which was used to make the particular PTP-SN is denoted as the

corresponding PTP polypeptide or corresponding wildtype PTP polypeptide. In certain embodiments, the PTP in a sulfenyl-amide form (PTP-SN) is any one of the classical PTPs or the DSPs described herein or known in the art, or a variant thereof, that has been oxidized to the inactive PTP-SN form. In a particular embodiment, the PTP is selected
 5 from PTP1B (SEQ ID NO:24, 26, 30) and DEP-1 (SEQ ID NO:38, 40). In certain other embodiments, the PTP is a DSP such as, for example, cdc14a (SEQ ID NO:85, 87, 89), cdc14b (SEQ ID NO:91, 93), cdc25a (SEQ ID NO:67, 69), cdc25b (SEQ ID NO:77, 79), cdc25c (SEQ ID NO:81, 83), or DSP-3/JSP-1 (SEQ ID NO:97).

The term "PTP-SS" means a PTP (a classical PTP or a DSP or a variant)
 10 as described herein, wherein the sulfur atom of the catalytic cysteine is covalently bonded to form a disulfide bond with the sulfur atom of a conformationally proximal or nearby cysteine residue. A PTP-SS may comprise a PTP known in the art as well as naturally-occurring splice-variants or mutants having a sequence selected from the group consisting of SEQ ID NO:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20 and 21,
 15 and may have a sequence disclosed herein and/or disclosed in Andersen et al. (2001 *Mol. Cell. Biol.* 21:7117). The PTP that forms a PTP-SS may be a PTP polypeptide variant having at least 70%, 80%, 85%, 90%, 95%, 98%, or 99% sequence identity to a sequence shown or described in Figure 6 herein, Figure 7 herein, or disclosed in Andersen et al. (2001 *Mol. Cell. Biol.* 21:7117), provided such PTP or PTP polypeptide variant
 20 comprises any one of the sequences set forth in SEQ ID Nos: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 106, 107, or 109; wherein the sulfur atom of the catalytic cysteine is covalently bonded to form a disulfide bond with the sulfur atom of a conformationally proximal or nearby cysteine residue. While all PTP-SN molecules comprise the signature catalytic cysteine motif sequence of SEQ ID NO:1, PTP-SSs of
 25 the invention comprise any of the motif sequences selected from:

His-Cys-(X) ₅ -Arg	(SEQ ID NO:2)
Val-His-Cys-(X) ₅ -Arg	(SEQ ID NO:3)
Ile-His-Cys-(X) ₅ -Arg	(SEQ ID NO:4)
Cys-(X) ₅ -Arg-Ser	(SEQ ID NO:5)

	Cys-(X) ₅ -Arg-Thr	(SEQ ID NO:6)
	Cys-(X) ₅ -Arg-Ser-Gly	(SEQ ID NO:7)
	Cys-(X) ₅ -Arg-Thr-Gly	(SEQ ID NO:8)
	His-Cys-(X) ₅ -Arg-Ser	(SEQ ID NO:9)
5	His-Cys-(X) ₅ -Arg-Thr	(SEQ ID NO:10)
	His-Cys-(X) ₅ -Arg-Ser-Gly	(SEQ ID NO:11)
	His-Cys-(X) ₅ -Arg-Thr-Gly	(SEQ ID NO:12)
	Val-His-Cys-(X) ₅ -Arg-Ser	(SEQ ID NO:13)
	Val-His-Cys-(X) ₅ -Arg-Ser-Gly	(SEQ ID NO:14)
10	Val-His-Cys-(X) ₅ -Arg-Thr	(SEQ ID NO:15)
	Val-His-Cys-(X) ₅ -Arg-Thr-Gly	(SEQ ID NO:16)
	Ile-His-Cys-(X) ₅ -Arg-Ser	(SEQ ID NO:17)
	Ile-His-Cys-(X) ₅ -Arg-Ser-Gly	(SEQ ID NO:18)
	Ile-His-Cys-(X) ₅ -Arg-Thr	(SEQ ID NO:19)
15	Ile-His-Cys-(X) ₅ -Arg-Thr-Gly	(SEQ ID NO:20)
	[I/V]HCXAGXXR[S/T]G	(SEQ ID NO:106)
	C(X) ₅ -R[S/T]	(SEQ ID NO:107)
	and CS-(X) ₄ -R	(SEQ ID NO:109);

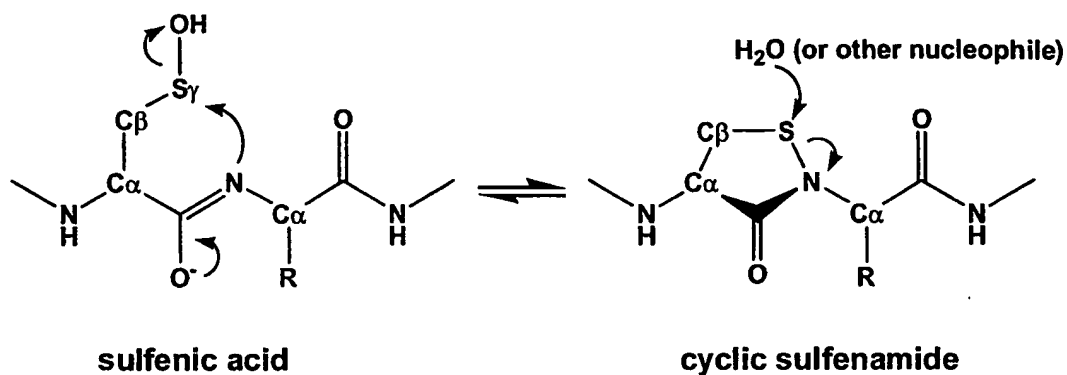
wherein X is any amino acid residue, natural or unnatural, and wherein the

20 sulfur atom of the catalytic cysteine is covalently bonded with the sulfur atom of a conformationally proximal or nearby cysteine residue to form a disulfide bond. The PTP polypeptide that is not in the SS form described herein but which was used to make the particular PTP-SS is denoted as the corresponding PTP polypeptide or corresponding wildtype PTP polypeptide that has been oxidized to form the sulfur-sulfur bond. In

25 certain embodiments, the PTP in a cyclic sulfenyl-amide form (PTP-SN) is any one of any one of the classical PTPs or the DSPs described herein or known in the art, or a variant thereof. In a particular embodiment, the PTP is selected from PTP1B (SEQ ID NO:24, 26, 30) and DEP-1 (SEQ ID NO:38, 40). In certain other embodiments, the PTP is a DSP such as, for example, cdc14a (SEQ ID NO:85, 87, 89), cdc14b (SEQ ID NO:91,

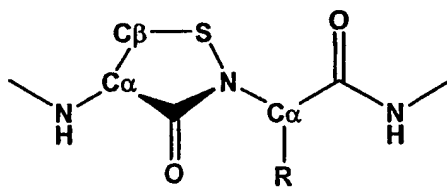
93), cdc25a (SEQ ID NO:67, 69), cdc25b (SEQ ID NO:77, 79), cdc25c (SEQ ID NO:81, 83), or DSP-3/JSP-1 (SEQ ID NO:97).

As used herein, the phrase “wherein the sulfur atom of the catalytic cysteine is covalently bonded to the main-chain nitrogen atom of the adjacent C-terminal
5 residue” means the following structures (II) or (V)



10

(V)



(II)

wherein R is the side chain (or side group) of the C-terminal adjacent
15 residue. The chemical composition and structure of the side chain of each amino acid are well known in the art (see also the linear structure presented in the table below).

Name	Linear Structure
Alanine (A)	CH ₃ -CH(NH ₂)-COOH
Arginine (R)	HN=C(NH ₂)-NH-(CH ₂) ₃ -CH(NH ₂)-COOH
Asparagine (N)	H ₂ N-CO-CH ₂ -CH(NH ₂)-COOH
Aspartic Acid (D)	HOOC-CH ₂ -CH(NH ₂)-COOH
Cysteine (C)	HS-CH ₂ -CH(NH ₂)-COOH
Glutamic Acid (E)	HOOC-(CH ₂) ₂ -CH(NH ₂)-COOH
Glutamine (Q)	H ₂ N-CO-(CH ₂) ₂ -CH(NH ₂)-COOH
Glycine (G)	NH ₂ -CH ₂ -COOH
Histidine (H)	NH-CH=N-CH=C-CH ₂ -CH(NH ₂)-COOH
Isoleucine (I)	CH ₃ -CH ₂ -CH(CH ₃)-CH(NH ₂)-COOH
Leucine (L)	(CH ₃) ₂ -CH-CH ₂ -CH(NH ₂)-COOH
Lysine (K)	H ₂ N-(CH ₂) ₄ -CH(NH ₂)-COOH
Methionine (M)	CH ₃ -S-(CH ₂) ₂ -CH(NH ₂)-COOH
Phenylalanine (F)	Ph-CH ₂ -CH(NH ₂)-COOH
Proline (P)	NH-(CH ₂) ₃ -CH-COOH
Serine (S)	HO-CH ₂ -CH(NH ₂)-COOH
Threonine (T)	CH ₃ -CH(OH)-CH(NH ₂)-COOH
Tryptophan (W)	Ph-NH-CH=C-CH ₂ -CH(NH ₂)-COOH
Tyrosine (Y)	HO-Ph-CH ₂ -CH(NH ₂)-COOH
Valine (V)	(CH ₃) ₂ -CH-CH(NH ₂)-COOH

Portions of two PTP polypeptide sequences are regarded as having corresponding amino acid sequences, regions, fragments or the like, based on a convention of numbering one PTP sequence according to amino acid position number, and then aligning the sequence to be compared in a manner that maximizes the number of amino acids that match or that are conserved residues, for example, that remain polar (*e.g.*, D, E, K, R, H, S, T, N, Q), hydrophobic (*e.g.*, A, P, V, L, I, M, F, W, Y), or neutral (*e.g.*, C, G) residues at each position. A variety of criteria known to those skilled in the art indicate whether amino acids at a particular position in a peptide or polypeptide are similar. For example, a similar amino acid or a conservative amino acid substitution is

one in which an amino acid residue is replaced with an amino acid residue having a similar side chain, which include amino acids with basic side chains (e.g., lysine, arginine, histidine); acidic side chains (e.g., aspartic acid, glutamic acid); uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine, histidine); nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan); beta-branched side chains (e.g., threonine, valine, isoleucine), and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan). Proline, which is considered more difficult to classify, shares properties with amino acids that have aliphatic side chains (e.g., Leu, Val, Ile, and Ala). In certain circumstances, substitution of glutamine for glutamic acid or asparagine for aspartic acid may be considered a similar substitution in that glutamine and asparagine are amide derivatives of glutamic acid and aspartic acid, respectively.

Alignment may be achieved by comparing sequences, aligning the signature catalytic cysteine motif and other invariant or highly conserved amino acid residues, using computer algorithms well known to those having ordinary skill in the art, such as GENEWORKS, Align or the BLAST algorithm (Altschul, *J. Mol. Biol.* 219:555-565, 1991; Henikoff and Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915-10919, 1992), which is available at the NCBI website (see Internet>URL:<http://www.ncbi.nlm.nih.gov/cgi-bin/BLAST>) (see also Andersen et al. (2001), *supra*; Andersen et al. (2004), *supra*). Other sequence alignment algorithms, with which those having ordinary skill in the art will be familiar, may also be used.

A DNA sequence encoding a candidate PTP that is to be mutated as provided herein, or a portion, region, fragment or the like, may correspond to a known wildtype PTP-encoding DNA sequence according to a convention for numbering nucleic acid sequence positions in the known wildtype PTP-encoding DNA sequence, whereby the candidate PTP DNA sequence is aligned with the known PTP-encoding DNA such that at least 70%, and preferably at least 80%, 85%, at least 90%, at least 95%, or at least 98% of the nucleotides in a candidate PTP DNA-encoding sequence of at least 20 consecutive nucleotides are identical to a known PTP-encoding DNA sequence.

Modification of DNA may be performed by a variety of methods, including site-specific or site-directed mutagenesis of DNA encoding the PTP and the use of DNA amplification methods using primers to introduce and amplify alterations in the DNA template, such as PCR splicing by overlap extension (SOE). Site-directed
5 mutagenesis is typically effected using a phage vector that has single- and double-stranded forms, such as M13 phage vectors, which are well-known and commercially available. Other suitable vectors that contain a single-stranded phage origin of replication may be used (*see, e.g.,* Veira et al., *Meth. Enzymol.* 15:3, 1987). In general, site-directed mutagenesis is performed by preparing a single-stranded vector that encodes the protein
10 of interest (*e.g.,* a member of the PTP family). An oligonucleotide primer that contains the desired mutation within a region of homology to the DNA in the single-stranded vector is annealed to the vector followed by addition of a DNA polymerase, such as *E. coli* DNA polymerase I (Klenow fragment), which uses the double stranded region as a primer to produce a heteroduplex in which one strand encodes the altered sequence and
15 the other the original sequence. Additional disclosure relating to site-directed mutagenesis may be found, for example, in Kunkel et al. (*Methods in Enzymol.* 154:367, 1987); and in U.S. Patent Nos. 4,518,584 and 4,737,462. The heteroduplex is introduced into appropriate bacterial cells, and clones that include the desired mutation are selected. The resulting altered DNA molecules may be expressed recombinantly in appropriate
20 host cells to produce the modified protein.

The term "isolated" as used herein refers to removal of a molecule such as a PTP or PTP-SN from its natural source, environment or milieu (*e.g.,* removal of a protein from an intact cell source), and the term "purified" as used herein means that the PTP or PTP-SN is essentially free of association with other proteins or polypeptides, for example,
25 as a purification product of recombinant host cell culture, or as a purified product from a non-recombinant source. An "isolated" polypeptide therefore is one that is removed from its original environment. Preferably, such polypeptides are at least about 90% pure, at least about 95% pure, or at least about 99% pure, for example, where such a degree of purity refers to the percentage of detectable PTP or PTP-SN that is present in a preparation

relative to other detectable polypeptides. The term “substantially purified” or “substantially isolated” as used herein means a mixture that contains a molecule such as a PTP or a PTP-SN that is essentially free of association with other proteins or polypeptides, but for the presence of known proteins that can be removed using conventional methods, such as by affinity chromatography with a specific antibody, and which substantially purified or substantially isolated PTP or PTP-SN retains its biochemical characteristics as described herein or retains its conformational properties.

The methods described herein may be used for identifying compounds or agents that bind to the oxidized cyclic sulfenyl-amide form of a PTP and prevent such PTP-SN from returning to its active cysteine thiol-containing state. Once identified, such agents or compounds should be useful for potentiating, stimulating, increasing the flux or signal through a pathway that is regulated by that PTP, and which in certain preferred embodiments is contemplated to be a pathway that is negatively regulated by the PTP. For example, a compound may be identified by crystallizing an isolated PTP-SN and then soaking (or incubating, immersing, exposing, bathing, contacting or otherwise administering) the crystal in a solution containing a candidate compound and determining if the compound binds to the PTP-SN according to X-ray crystallography methods described herein and known in the art (*see, e.g., Johnson and Blundell, Protein Crystallography* (Academic Press 1976); Blundell et al. *Nat. Rev. Drug Discov.* 1:45-54 (2002)). Other methods for determining whether a compound binds to a PTP-SN include isothermal titration calorimetry in the solution state (Weber et al., *Curr. Opin. Struct. Biol.* 13:115-21 (2003); Ward et al., *Prog. Med. Chem.* 38:309-76 (2001); Cliff et al., *J. Mol. Recognit.* 16:383-91 (2003)) or surface plasmon resonance (*e.g., BIAcore, Biosensor, Piscataway, NJ*).

OXIDATION/REDUCTION OF PTPs

Methods to make and test PTP-SN or PTP-SS forms are described herein. Because the inventors have discovered that the previously unknown, inactive cyclic-sulfenylamide form of a PTP is based on oxidation of amino acids within the $-C(X)_5-R-$

motif (SEQ ID NO:1) (the PTP signature catalytic cysteine motif), a substantial number of known and distinct PTPs may also be oxidized into the inactive cyclic-sulfenylamide form (PTP-SN) or PTP-SS form. Thus, any PTP may be used to make a PTP-SN or PTP-SS form including, without limitation, the classical PTPs as described by Andersen et al. (2001) (*supra*) and Andersen et al., 2004 (*supra*) and DSPs, for example, phosphatases such as PTP-eta, PTP-epsilon, DEP-1 (CD148), SHP2, SHP1, cdc25a, cdc25b, cdc25c, cdc14a, cdc14b, DSP-2, DSP-3/JSP-1, DSP-4, DSP-5, DSP-6, DSP-7, DSP-8, DSP-9, DSP-10, DSP-11, DSP-12, DSP-13, DSP-14, DSP-15, DSP-16, DSP-17, DSP-18, CD45, etc. Such PTPs, whether in isolated or purified form or in whole cells, may be subjected to oxidizing conditions as described herein, including an oxidizing agent, for example, hydrogen peroxide, and/or with another agent that directly or indirectly promotes reactive oxygen species (ROS) generation, under conditions and for a time sufficient to permit the production of the PTP-SN or PTP-SS form.

Oxidation of a PTP to the PTP-SN form results in an oxidatively modified PTP that is incapable of its normal recognition or and/or binding to a PTP substrate, thus inhibiting its catalytic dephosphorylation activity. Oxidation conditions resulting in the PTP-SN form may be reversible and, thus, may be controlled such that when the catalytic cysteine in the inactive PTP-SN form is reduced, for instance by thiols, the PTP can be regenerated in an active enzymatic state. Exposure of the PTP-SN form to increasing concentrations of ROS, or to an oxidizing agent, may result, however, in irreversible oxidation to sulfinic (-SO₂) and sulfonic (-SO₃) acid forms of the PTP. As described in detail herein, analytical techniques such as protein crystallography and mass spectrometry analyses (such as matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry) may be used for determining whether a PTP is in the PTP-SN form or in an irreversibly oxidized form. Electron density maps may be calculated by Fourier transformations and may be visualized by using crystallography software programs with which those skilled in the art are familiar (*e.g.*, REFMAC (Collaborative Computational Project No. 4. The CCP4 suite: programs for protein crystallography, *Acta Crystallogr. D* 50:670-63 (1994)); XtalView, McRee, *J. Molecular Graphics* 10: 44-

46 (1992)). Determining oxidation conditions under which a PTP is reversibly oxidized or irreversibly oxidized may also be determined by additional methods described herein. These analyses include, for example, determining the oxidation conditions under which a substrate trapping mutant of the corresponding wildtype PTP is oxidized to the sulfenyl-
5 amide state such that the substrate trapping mutant has a reduced capability (total loss or partial reduction) to bind to or to form a complex with its PTP substrate, and determining under what particular oxidation conditions the substrate trapping mutant PTP's decreased (or absent) substrate binding (or decreased or absent complex formation) may be reversible, and under what oxidation conditions such substrate binding may be
10 irreversible.

As a representative example to illustrate the mechanism of the reversibility of redox regulation of a PTP, X-ray crystallography and mass spectrometry were integrated to monitor the structural changes of the PTP, PTP1B, that occur upon oxidation of its catalytic site cysteine. Efforts were undertaken to determine the structure
15 of PTP1B with the catalytic cysteine in the physiologically relevant, reversibly oxidized, Cys-SOH state. Surprisingly, however, by incubating the PTP1B enzyme with stoichiometric amounts of H_2O_2 , formation of sulfenic acid was not observed, but instead an unexpected modification of the catalytic site Cys residue was observed, a cyclic-sulfenyl-amide species as described herein (Fig 1A). Furthermore, the structure of
20 PTP1B was determined at several stages during a time course of oxidation in response to H_2O_2 . Unexpectedly, only conversion to the novel cyclic-sulfenyl-amide intermediate was detected, and not the Cys-SOH state (Fig. 1B). The electron density maps were consistent with a mixture being present of both reduced and cyclic-sulfenyl-amide conformational states. Importantly, there was no definitive evidence of a sulfenic acid
25 structure, indicating according to non-limiting theory that the rate of formation of this intermediate may have been ratelimiting in the generation of the cyclic-sulfenyl-amide species. Alternative conformation refinement using REFMAC (Collaborative Computational Project No. 4. The CCP4 suite: programs for protein crystallography, *Acta Crystallogr. D* 50:670-63 (1994)) accounted for the observed electron density maps

and allowed the relative proportions of the reduced and sulfenyl-amide states to be estimated. The 75-minute time-point was consistent with an almost equal mixture of the reduced and sulfenyl-amide forms of PTP1B, whereas at 40 min, approximately 25% of the enzyme had converted to the sulfenyl-amide state. After a 16-hour incubation, most
5 of the sulfenyl-amide species was oxidized to sulfonic acid, and this structure of PTP1B resembled PTP1B-SO₃ generated using pervanadate, a strong oxidizing agent. In these structures, the PTP and pTyr loops adopted the closed conformation, identical to reduced PTP1B.

The oxidation of the catalytic Cys to the cyclic-sulfenyl-amide state
10 resulted in profound changes in the structure of the active site with inhibition of activity. PTP mediated catalysis occurs via a two-step mechanism involving a thiophosphate intermediate of the catalytic Cys. The active site of PTP1B is present as a pronounced cleft on the surface of the protein. Its base is formed by the PTP loop, which contains the catalytic Cys215 and residues of the PTP signature motif (residues 214-222) (Barford et
15 al., *Annu. Rev. Biophys. Biomol. Struct.* 27:133-64 (1998); Denu et al., *Biochemistry* 37:5633-42 (1998)). The sides of the cleft are formed by three motifs: the pTyr loop, containing Tyr46, which defines the depth of the cleft (Jia et al., *Science* 268:1754-58 (1995)); the Q loop containing Gln262, which mediates hydrolysis of the cysteinyl phosphate catalytic intermediate (Pannifer et al., *J. Biol. Chem.* 273:10454-62 (1998));
20 and the WPD loop, which moves to close the active site following substrate binding and contains the essential Asp181 residue that functions in both stages of catalysis. In the catalytically active, reduced form of PTP1B, the PTP loop adopts a cradle conformation to bind the substrate phosphate and position the thiol group of the Cys for nucleophilic attack onto the substrate (Barford et al. (1998) *supra*; Jia et al. (1995), *supra*). The Sy-
25 atom of Cys215 accepts a hydrogen bond from the side chain of Ser222, and is within 3.6 Å of the main chain nitrogen atom of Ser216. In addition, the side chain of Tyr46 is directed towards the PTP loop and its phenolic hydroxyl group forms a hydrogen bond to the side chain of Ser216 of the PTP loop (Fig. 2A).

In the cyclic-sulfenyl-amide oxidized state of PTP1B (PTP1B-SN), a covalent bond formed between the S γ -atom of Cys215 and the main chain nitrogen atom of Ser216 (Fig. 2B). Electron density maps in the region of the PTP loop indicated well-defined continuous density bridging the S γ -atom of Cys215 and the main chain nitrogen atom of Ser216 (Fig. 1). Formation of this bond occurred via a nucleophilic attack of the
5 main-chain nitrogen atom of Ser216 onto the electrophilic sulfur atom of the labile sulfenic acid, with concomitant release of water (Fig. 2D). Importantly, *Fo-Fc* electron density maps revealed that no additional oxygen atoms were attached to S γ of Cys215 in the sulfenyl-amide species (Fig. 1). This observation was consistent, by way of non-
10 limiting theory, with the occurrence of a nucleophilic substitution reaction (Fig. 2D). The resultant sulfenyl-amide covalent bond was a five-atom cyclic structure that has not been previously observed in proteins.

Conformational changes of the side chains of Cys215 and Ser216 accompanied generation of the sulfenyl-amide bond and triggered tertiary structural
15 changes in both the PTP and pTyr loops (Fig. 2C). Residues Ser216 to Arg221 underwent a dramatic change of conformation that flipped the PTP loop out of the catalytic site. Notably, Gly218 shifted by approximately 7 Å, and the helical conformation of the PTP loop in reduced PTP1B (Gly218 is left-handed) converted to a reverse β -hairpin conformation, which imposed strain on the main-chain conformation of
20 Arg221. The trigger for the conformational change of the PTP loop resulted from the loss of the Cys215 – Ser222 hydrogen bond and conformational constraints on the main chain of the PTP loop imposed by the sulfenyl-amide bond. The conformational shift of the Ser216 side chain in the cyclic-sulfenyl-amide structure disrupted the hydrogen bond to the hydroxyl group of Tyr46 and this promoted a displacement of Tyr46 to a solvent
25 exposed position, accompanied by shifts of the entire pTyr recognition loop. Apart from the conformational changes of the PTP and pTyr loops, and side chain of Gln262 of the Q-loop, other regions of the structure remained unchanged on oxidation (Fig. 2C). The open conformation of the PTP loop in the sulfenyl-amide state exposed the S γ -atom of Cys215, enhancing its accessibility for modification by thiols. Significantly, incubating

crystals of PTP1B-SN with either DTT or glutathione demonstrated quantitative reduction of the sulfenyl-amide cysteine, and a conformational change of both the PTP and pTyr loops to their catalytically active conformations. Interestingly, in PTP1B-SO₃, generated either using pervanadate, a strong oxidizing agent, or prolonged exposure to
5 H₂O₂, the PTP and pTyr loops adopted the closed conformation.

In following the time-course of oxidation induced by H₂O₂ in the crystal of PTP1B, it was noted that the sulfenic acid (SOH) form of Cys 215 was rapidly converted to a cyclic-sulfenyl-amide species, facilitated according to non-limiting theory by the close proximity of the S_γ atom of Cys215 to the polarized amide nitrogen of Ser216 (Figs.
10 1 and 2) (*see* Barford et al., *Science* 263:1397-404 (1994)). To explore the oxidation of PTP1B in solution, the protein was subjected to varying amounts of H₂O₂ then, following trypsinisation, the mass of the active site Cys-containing peptide was examined by MALDI-TOF mass spectrometry (Fig. 3A). At high concentrations of H₂O₂, which caused irreversible oxidation of the active site Cys, a shift in M_r of +32 or +48 Da was
15 readily detected, equivalent to the formation of the sulfinic (Cys-SO₂) or sulfonic acid (Cys-SO₃) derivatives, respectively. However, at the lower concentrations of H₂O₂, which induced reversible oxidation of PTP1B, formation of Cys215-SOH was not detected. Similar results were found for the intact protein. In the PTP1B C215S mutant, in which the active site Cys was replaced by Ser, there was no change in the mass of this
20 peptide at any concentration of H₂O₂ (Fig. 3A). To test whether this failure to detect the sulfenic acid derivative was due to its rapid conversion to another species, such as sulfenyl-amide, pulse-chase analysis with H₂¹⁸O₂ was performed. Incubation of PTP1B with a 1000-fold molar excess "heavy" H₂¹⁸O₂ or "light" H₂¹⁶O₂ (50 mM), which resulted in irreversible inactivation of the enzyme (Fig. 3B, left panel), led to production of
25 sulfonic acid derivatives with a mass increase of +54 (all ¹⁸O) or +48 (all ¹⁶O) respectively (Fig. 3B, right panel). However, when PTP1B was pre-incubated with lower levels of H₂¹⁸O₂, which led to reversible inhibition of PTP1B, and then chased with a >100-fold excess of H₂¹⁶O₂, production of a sulfonic acid derivative of mass +50 (1, ¹⁸O and 2, ¹⁶O) was not detected, but only +48 (all ¹⁶O) (Fig. 3B). This observation was

consistent with a mechanism, according to non-limiting theory, that at concentrations of peroxide that resulted in reversible inhibition of PTP1B, oxygen was rapidly eliminated from sulfenic acid, the first oxidized form of the active site Cys, to generate a more stable derivative, such as the sulfenyl-amide species (Fig. 2). Importantly, this species was
5 formed in the presence of thiols.

Together, crystallographic and pulse-chase mass spectrometry data established a model for the inter-relationship of PTP1B oxidation states (Fig. 4A). Oxidation to the sulfenyl-amide state would be anticipated to inhibit the PTP's activity in a reversible manner, with the chemical and structural characteristics of the sulfenyl-amide
10 species both suppressing irreversible oxidation to sulfinic and sulfonic acids and permitting modification of Cys215 by thiols to regenerate an active state of the enzyme. In order to examine the effects of the oxidation-mediated structural changes on the function of PTP1B, a substrate trapping mutant form of the PTP (Flint et al., *Proc. Natl. Acad. Sci USA* 94:1680-85 (1997)) was incubated together with the insulin receptor
15 kinase (IRK), a physiological substrate of PTP1B (Elchelbly et al., *Science* 283:1544-48 (1999); Klamann et al., *Mol. Cell Biol.* 20:5479-89 (2000)), and ATP in the presence of increasing concentrations of H_2O_2 . After incubation, complexes containing PTP1B were immunoprecipitated and blotted with antibodies to phosphotyrosine (Fig. 4B). At low concentrations of H_2O_2 , which did not result in oxidation of PTP1B, a complex of the
20 substrate trapping mutant and the IRK was recovered. However, at concentrations of H_2O_2 that resulted in oxidation, binding of PTP1B to the IRK was disrupted, consistent with inhibition of substrate recognition by oxidation. Interestingly, at these higher concentrations of H_2O_2 , enhanced tyrosyl phosphorylation of PTP1B by the IRK was observed. Consistent with the oxidation-induced structural changes in PTP1B in which
25 Tyr46 adopted a solvent exposed position, phosphorylation of a PTP1B mutant, in which Tyr46 was changed to Phe, was attenuated relative to the wild type enzyme (Fig. 4C). Such phosphorylation raises the possibility of an additional tier of control over the redox regulation of PTP1B.

It has been proposed that the catalytic cysteines of cdc25, the low molecular weight (Mr) PTP and the tumor suppressor phosphatase PTEN are protected from irreversible oxidation by disulfide bond formation with vicinal cysteines (*i.e.*, cysteine residues that occupy the same local or nearby space in a three-dimensional structure) (Fauman et al., *Cell* 93:617-25 (1998); Caselli et al., *J. Biol. Chem.* 273:32554-60 (1998); Lee et al., *J. Biol. Chem.* 277:20336-42 (2002)); however, the tyrosine-specific PTPs do not contain equivalent vicinal thiols at their active sites with the exception of the PTP-PEST subgroup, which does have vicinal cysteine residues as determined by amino acid sequence alignments with PTP1B and KAP (*see* Andersen et al., (2001) *supra* and Andersen et al., (2004), *supra*). The present disclosure, however, describes a novel alternative mechanism to prevent irreversible PTP oxidation, which may also facilitate formation of glutathionylated PTP derivatives (*e.g.*, PTP1B, Barrett et al., *Biochemistry* 38:6699-705 (1999)), thus allowing redox-dependent regulation of these enzymes (Fig. 4A). The inventors are the first to demonstrate a covalent modification of a main-chain peptide group and to demonstrate the potential reactivity of the amide nitrogen atom. The associated conformational changes of PTP1B as described herein illustrate how ROS function as second messengers by mediating cysteine oxidation coupled to an allosteric transition of protein structure. The invention embodies a novel oxidation-dependent post-translational modification, which may have implications for understanding mechanisms of redox signaling that are important in the regulation of gene expression and signal transduction (Herrlich et al., *Biochem. Pharmacol.* 59:35-41 (2000); Kim et al., *Cell* 109:383-96 (2002)).

In another embodiment, the crystalline coordinates of a PTP-SN (*e.g.*, PTP1B-SN) may be used in structure-based screening for rational drug design (*see, e.g.*, Blundell et al., *Nat. Rev. Drug Discov.* 1:45-54 (2002); Carr et al., *Drug Discov. Today* 7: 522-27 (2002); Stewart et al., *Drug Discov. Today* 7:187-96 (2002); Rowland, R.S. *Curr. Opin. Drug Discov. Devel.* 5:613-19 (2002); *see also, e.g.*, Fejzo et al., *Curr. Top. Med. Chem.* 3:81-97 (2003); Hajduk et al., *J. Med. Chem.* 42:2315-17 (1999); van Dongen et al., *Drug Discov. Today* 7:471-78 (2002)). For example, coordinates may be used in

computer-aided drug design, using software and hardware readily available in the art. Further, the invention contemplates a recordable medium or computer-readable medium comprising the crystal coordinates of PTP1B-SN as shown in the Tables. Such recordable media and their uses as well as methods and materials for implementing
5 rational drug design are well known in the art, for example, as disclosed in WO 200295035 A1; WO 2003006674 A1; and WO 2003006987 A1. For instance, computer-readable media include magnetic media and optically-readable media. Examples of magnetic media include a hard or fixed drive, a random access memory (RAM) chip, a floppy disk, digital linear tape (DLT), a disk cache, and a ZIP disk. Optically-readable
10 media are exemplified by compact discs (*e.g.*, CD-read only memory (ROM), CD-rewritable (RW), and CD-R recordable), and digital versatile/video discs (DVD) (*e.g.*, DVD-ROM, DVD-RAM, and DVD+RW)).

In one embodiment, a method is provided for determining a three-dimensional structure for a target PTP1B-SN and also provided is a computer system or
15 computer-readable media containing (a) atomic coordinate data listed in the specification, which defines the three-dimensional structure of PTP1B-SN, or at least its selected coordinates; (b) structure factor data derived from the atomic coordinate data cited above; (c) a Fourier transform of the atomic coordinate data cited above; (d) atomic coordinate data of a target PTP1B-SN generated by homology modeling of the target based on the
20 data listed in the specification; (e) atomic coordinate data of a target PTP1B-SN generated by interpreting X-ray crystallographic data or NMR data by reference to any of the data listed in the specification; or (f) structure factor data derived from the atomic coordinate data of (c)-(e); and modeling the interaction between PTP1B-SN and an agent compound that modulates the PTP activity. In another embodiment, a method for rational
25 drug design may be used for identifying an agent compound capable of altering the enzymatic activity of PTP1B, comprising (a) introducing information defining the conformation of a PTP1B-SN inhibitor complex molecule into a suitable computer program (the conformation identity defined by the coordinates given herein) that displays the three-dimensional structure of such PTP1B-SN; (b) creating a three-dimensional

structure of a test compound in the computer program; (c) displaying and superimposing the model of the test compound on the model of the PTP1B-SN; (d) assessing whether the test compound model fits spatially into a desired region of PTP1B-SN; (e) incorporating the test compound in a biological activity assay for PTP1B; and (f) determining whether the test compound alters or modulates enzymatic activity of PTP1B in the assay. Such rational drug design methods may also be used for any other PTP-SN or mutant PTP of interest described herein.

MUTANT PTPs THAT CONFORMATIONALLY RESEMBLE PTP-SN

In another embodiment, the present invention relates to the discovery that a mutant PTP with two mutations in the signature catalytic cysteine site motif has a three-dimensional structural conformation that is highly similar (or substantially similar) to the three-dimensional conformation of the herein described PTP-SN form of a corresponding PTP. For example, a PTP1B cysteine215-to-alanine (CA or C215A) and serine216-to-alanine (SA or S216A) double mutant results in a conformational change to the PTP1B polypeptide. Such double mutant may operate as a stable surrogate for the herein described PTP-SN molecule. Hence, assays useful for screening for agents or compounds or antibodies that bind to the double mutant would also likely identify agents, compounds, and/or antibodies that bind to the PTP-SN form. Related embodiments of the invention also contemplate antibodies or other binding proteins capable of specifically binding to such a double mutant PTP (e.g., double mutant PTP1B) and their uses, for instance, as detection reagents in cells.

In one embodiment, the double mutant PTP comprises a substitution of the cysteine residue (which is the catalytic cysteine) in the signature catalytic cysteine site motif (-C-(X)₅-R-, SEQ ID NO:1) and a substitution of the residue that is the adjacent C-terminal residue to the cysteine residue. In a certain embodiment, the double mutant PTP comprises a substitution of the cysteine residue in the signature catalytic site motif (-C-(X)₅-R-, SEQ ID NO:1) and a substitution of a serine residue that is the adjacent C-terminal residue to the cysteine residue (-C-S-(X)₄-R-, SEQ ID NO:109). A double

mutant PTP may be derived from a classical PTP as described herein (see also Andersen et al. (2001), *supra*; Andersen et al. (2004), *supra*), the signature catalytic site motif of which is the amino acid sequence -H-C-S-X-G-X-G-R-X-G- (SEQ ID NO:21), wherein in the double mutant, the catalytic cysteine and the serine residue that is the adjacent C-terminal residue to the catalytic cysteine are replaced. The cysteine residue in the signature catalytic site motif may be replaced with an amino acid including alanine, aspartic acid, glutamic acid, valine, leucine, isoleucine, proline, phenylalanine, tryptophan, methionine, glycine, serine, threonine, tyrosine, asparagine, glutamine, lysine, arginine, or histidine or other natural or non-natural amino acids known in the art including derivatives, variants and the like. Non-natural amino acids may be derived from naturally occurring amino acids and may be substituted in a PTP polypeptide sequence according to methods known in the art (*see, e.g.*, Hosaka et al., *Curr. Opin. in Chem. Biol.* 6:809-15 (2002); Evrard et al., *Acta Cryst.* D55:430-35 (1999); Sisido et al., *Appl. Microbiol. Biotechnol.* 57:274-81 (2001)).

In a particular related embodiment, the catalytic cysteine residue of the PTP is replaced with an alanine residue. By way of example, a double mutant PTP1B (SEQ ID NO:110) that has a structural conformation similar to the structural conformation of the PTP1B-SN form comprises a substitution of the cysteine residue that is located at position 215 in the wildtype PTP1B amino acid sequence (SEQ ID NO:24, 26, 30) with an alanine residue and a substitution of the serine residue that is located at position 216 in the wildtype PTP1B amino acid sequence (SEQ ID NO:24, 26, 30) with an alanine residue. The PTP polypeptide that does not contain the mutations described herein but which was used to make the double mutant PTP is denoted as the corresponding PTP polypeptide or corresponding wildtype PTP polypeptide. In another embodiment, the PTP in a double mutant form is DEP-1.

The structural conformation of the double mutant PTP polypeptides, similar to the conformational changes observed in a PTP-SN, includes the tertiary structural changes in both the PTP and pTyr loops. The PTP loop flips out of the catalytic site, and the helical conformation of the PTP loop converts to a reverse β -hairpin

conformation, which imposes strain on the main-chain conformation of the arginine residue in the signature catalytic cysteine motif. The loss of the hydrogen bond between the catalytic cysteine, which has been replaced, and another residue (such as the residue that is the C-terminal residue adjacent to the arginine in the signature catalytic cysteine motif, which frequently is a serine or threonine residue (see Figures 6 and 7)) places conformational constraints on the main chain of the PTP loop. The substitution of the serine that is the adjacent C-terminal residue to the catalytic cysteine disrupts the hydrogen bond to the hydroxyl group of a tyrosine residue (for example, the Tyr46 residue in PTP1B), and this promotes a displacement of the tyrosine to a solvent exposed position, accompanied by shifts of the entire pTyr recognition loop. Apart from the conformational changes of the PTP and pTyr loops, and the side chain of a residue in the Q-loop (for example, Gln262 of the Q-loop in PTP1B), other regions of the structure remain unchanged.

Conformational changes of a double mutant PTP may be determined by X-ray crystallography, mass spectrometry, and computer molecular modeling and other techniques described herein and known in the art. Conformational changes may also be detected by using antibodies that specifically recognize a conformational epitope that is formed by a double mutant PTP but that is not present in the corresponding wildtype PTP. A conformational epitope or conformational antigenic determinant may be composed of amino acid residues from separated portions of the primary amino acid sequence that are spatially juxtaposed in the three-dimensional structure of a folded protein. A conformational epitope may also be composed of two or more adjacent amino acids in the primary amino acid sequence and other amino acids that are spatially juxtaposed in the three-dimensional structure to the adjacent amino acids.

Antibodies may be prepared according to methods described herein and known in the art that bind specifically to a double mutant PTP but do not bind to the corresponding wildtype PTP, and other antibodies may be prepared that bind to the wildtype PTP polypeptide but that do not specifically bind or recognize the double mutant PTP polypeptide. In a particular embodiment, the antibodies that specifically bind to a

double mutant PTP also specifically bind to the PTP in the cyclic sulfenyl amide form (PTP-SN) form. An antibody that specifically binds to the PTP-SN form may thus inhibit, hinder, protect, or prevent the PTP-SN from being reduced to the catalytically active form of the PTP. Such an antibody may be useful as a therapy for treating diseases or conditions associated with a signal transduction pathway in which the PTP is involved. For instance, without wishing to be bound by theory, an antibody or antigen binding fragment thereof that binds specifically to the PTP-SN form of PTP1B may trap the PTP1B in an inactive form and thus promote insulin signaling, which is useful for treating diabetes.

Immunodetection methods described herein and known to a skilled artisan may be routinely performed to identify such antibodies. For example, a conformational epitope may be identified by a monoclonal antibody that specifically binds to its cognate polypeptide antigen when the antigen is in its native state, but that fails to bind to the antigen when the conformation of the polypeptide antigen is disrupted, for instance when the antigen has been denatured.

PTP ASSAYS

As described herein, the presently disclosed sulfenyl amide (or cyclic-sulfenyl-amide) form of PTPs (PTP-SN), which result from oxidative PTP modification, lack PTP catalytic activity and also lack PTP substrate binding activity. As also noted herein, the oxidative PTP modification that gives rise to PTP-SN is reversible, such that subsequent reduction of the functionally inactive PTP-SN can yield an active PTP. Suitable assay conditions for determining PTP-mediated catalytic dephosphorylation of a PTP substrate tyrosine phosphorylated polypeptide can be readily determined without undue experimentation by a skilled person, based on the disclosure herein and known methods and properties of PTPs. Enzymatic activity assays are known in the art and may be modified according to the teachings herein; for example, assays of PTP activity using a tyrosine phosphorylated ³²P-labeled substrate are described in Flint et al. (1993 *EMBO J.* 12:1937-1946). For instance, a substrate may be dephosphorylated *in vitro* by incubating

a PTP with a detectably labeled substrate peptide in a suitable buffer (*e.g.*, Tris, pH 7.5, 1 mM EDTA, 1 mM dithiothreitol, 1 mg/mL bovine serum albumin) for 10 minutes at 30°C. In general, and depending upon the particular assay type selected (*e.g.*, with regard to sensitivity and detection limits that may vary as a function of the reporter signal that is monitored, and further with regard to assay formats such as conventional test tubes or high throughput formats such as 96-well, 384-well or other high throughput microplates) the amounts of the reaction components may range from about 0.5-10 pg to about 50-500 ng of PTP polypeptide and from about 0.5 ng (0.1 ng for FP assays) to about 10 µg of substrate polypeptide. The extent of substrate dephosphorylation may generally be monitored by determining a fluorescence energy signal as described, for example, in WO 01/61031 using fluorescence polarization or FRET.

It is contemplated that the present invention will be of significant value in high throughput screening; *i.e.*, in automated screening of a large number of candidate compounds for activity against one or more PTPs. It has particular value, for example, in screening synthetic or natural product libraries for compounds that exhibit activity in affecting PTP binding and PTP catalysis in binding and catalytic assays as described herein. The methods described herein are therefore amenable to automated, cost-effective high throughput drug screening and have immediate application in a broad range of pharmaceutical drug development programs. In a preferred embodiment of the invention, the compounds to be screened are organized in a high throughput screening format such as a 96-well plate format, or other regular two dimensional array, such as a 384-well, 48-well or 24-well plate format or an array of test tubes. It is preferred, for example, that an automated apparatus for use according to high throughput screening embodiments is under the control of a computer or other programmable controller. The controller can continuously monitor the results of each step of the process and can automatically alter the testing paradigm in response to those results.

AGENTS

As noted above, the invention is directed in part to a method for identifying an agent that hinders or modulates the reduction of a PTP-SN or PTP-SS (throughout this section, the teachings apply to PTP-SS as well as PTP-SN), by
5 combining a candidate agent such as a test compound with a PTP-SN to form a compound:PTP-SN composition, exposing the compound:PTP-SN composition to a reducing agent and also separately reducing the PTP-SN in the absence of the test compound, and evaluating the effect of the candidate agent on the phosphatase activity using, for example, a PTP activity assay described herein. An alteration in phosphatase
10 activity (*e.g.*, statistically significant increase or decrease) can be determined and would, in the case of a compound that hinders or modulates PTP-SN reduction, preferably be expected to manifest as an increase in the detectable PTP catalytic activity of the separately reduced PTP-SN, relative to that detected in the compound:PTP-SN composition following exposure to the reducing agent. Without wishing to be bound by
15 theory, according to such an assay, the test compound is believed to stabilize the PTP-SN (that is, stabilize the PTP-SN in the oxidized state) and thereby protect it from the reducing agent, which prevents conversion of the catalytically inactive PTP-SN to a catalytically active PTP. In general, a suitable amount of test compound (candidate agent) for use in such an assay ranges from about 0.001 μM to about 100 μM . The test
20 compound (candidate agent) may be an endogenous physiological substance, an antibody, or may be a natural or synthetic drug, including small organic molecules.

Candidate agents for use as test compounds in screening assays according to the present invention may be provided as "libraries" or collections of compounds, compositions or molecules. Such molecules typically include compounds known in the
25 art as "small molecules" and having molecular weights less than 10^5 daltons, preferably less than 10^4 daltons and still more preferably less than 10^3 daltons. For example, members of a library of test compounds can be administered to a plurality of samples in a high throughput screening array as provided herein, each containing at least one PTP-SN before and/or after exposure to reducing conditions sufficient to convert the PTP-SN to a

catalytically active PTP, and then assayed for the ability of the test compound (or candidate agent) to enhance or inhibit reduction of the PTP-SN. For example, identification of a compound that binds to a PTP-SN and that suppresses or decreases the rate at which the PTP-SN is reduced may be determined by a high throughput X-ray
5 crystallography method. Stepwise, sequentially, or simultaneously and in any order, for example, after preparing a crystal of the isolated PTP-SN, a test compound and reducing agent may be added to the crystallized PTP-SN, and then the rate at which the rate the PTP-SN is reduced may be determined. A preferred compound is one that binds to the PTP-SN form and suppresses reversion of the PTP-SN to the native PTP state (*i.e.*, via
10 reduction), thus inhibiting or blocking the capability of the PTP to bind and catalytically dephosphorylate a phosphorylated substrate. Compounds so identified as capable of influencing PTP-SN oxidation state (*e.g.*, stabilization) are valuable for therapeutic and/or diagnostic purposes since they permit treatment and/or detection of diseases associated with PTP activity. Such compounds are also valuable in research directed to molecular
15 signaling mechanisms that involve PTPs, and to refinements in the discovery and development of future PTP-active compounds exhibiting greater specificity.

Candidate agents further may be provided as members of a combinatorial library, which preferably includes synthetic agents prepared according to a plurality of predetermined chemical reactions performed in a plurality of reaction vessels. For
20 example, various starting compounds may be prepared employing one or more of solid-phase synthesis, recorded random mix methodologies and recorded reaction split techniques that permit a given constituent to traceably undergo a plurality of permutations and/or combinations of reaction conditions. The resulting products comprise a library that can be screened followed by iterative selection and synthesis procedures, such as a
25 synthetic combinatorial library of peptides (*see e.g.*, PCT/US91/08694, PCT/US91/04666, which are hereby incorporated by reference in their entireties) or other compositions that may include small molecules as provided herein (*see e.g.*, PCT/US94/08542, EP 0774464, U.S. 5,798,035, U.S. 5,789,172, U.S. 5,751,629, which are hereby incorporated by reference in their entireties). Those having ordinary skill in

the art will appreciate that a diverse assortment of such libraries may be prepared according to established procedures, and tested using PTPs and appropriate PTP substrates, according to the present disclosure.

Agents identified according to the methods described herein would be
5 useful in altering or modulating the reduction of the PTP-SN *in vivo*; and would be useful in treating a patient having a PTP-mediated condition or disease. Formulations of such agents into pharmaceutical compositions are well-known in the art and described herein.

ASSAYS UTILIZING PTP-SN, PTP-SS, OR DOUBLE MUTANT PTP

10 Compounds or agents that bind to the oxidized cyclic sulfenyl-amide form of a PTP and prevent it from returning to its active cysteine thiol containing state should be useful agents for potentiating, stimulating, increasing the flux or signal through a pathway that is negatively regulated by that PTP. For example, PTP1B is one such negative regulator of the insulin and leptin signaling pathways, and thus such compounds
15 would be predicted to improve insulin or leptin sensitivity in diabetic or obese patients. To identify such agents, a variety of assay methodologies using the PTP-SN, PTP-SS, or double mutant PTP molecules of the invention could be applied. Such methods fall into two general classes: (a) assays that measures the ability of a candidate agent to slow, hinder, impair, suppress or otherwise decrease (*e.g.*, in a statistically significant manner)
20 the restoration of enzyme activity to an oxidatively modified PTP (*e.g.*, PTP-SN or (PTP-SS) by a reducing agent, and (2) assays that measure binding of a candidate agent to the PTP-SN (or PTP-SS or mutant PTPs described herein) but without assessing the consequences of such binding on reappearance of enzyme activity. Any of the PTP polypeptides described herein and known in the art may be used in the methods and
25 assays described herein. Such PTPs include but are not limited to PTP1B (SEQ ID NO:24, 26, 30), cdc14a (SEQ ID NO:85, 87, 89), cdc14b (SEQ ID NO:91, 93), cdc25a (SEQ ID NO:67, 69), cdc25b (SEQ ID NO:77, 79), cdc25c (SEQ ID NO:81, 83), DSP-3/JSP-1 (SEQ ID NO:97), and DEP-1 (SEQ ID NO:38, 40).

In one embodiment, the desired PTP-SN or PTP-SS, as described herein, may be produced or obtained in a substantially purified or substantially isolated form, or in an isolated or purified form, by using methods described herein or other means known in the art that provide controlled oxidation of the catalytic cysteine. Throughout this section, the term "PTP-SN" is used to illustrate certain assays of the invention, but it is understood that PTP-SN, for such purposes, may refer interchangeably to any of PTP-SN, PTP-SS, or the mutant PTPs described herein (with the exception being that restoration of catalytic activity by treatment with a reducing agent would not be expected using the mutant PTP). A representative assay comprises the following steps: (a) contacting (combining, mixing, adding together, or otherwise introducing a PTP-SN to a test compound to form a composition) the PTP-SN with a candidate agent, for example, a test compound that is a small organic molecule, (b) adding a reducing agent to the agent:PTP-SN composition (the composition being a mixture of the agent and PTP-SN in which a portion of or all of the agent present in the mixture may form a complex with a portion or all of the PTP-SN); non-limiting examples of reducing agents include the thiol-containing compounds such as beta-mercaptoethanol, dithiothreitol (DTT), dithioerythritol (DTE) or glutathione, or non-thiol reducing agents such as phosphines (e.g., tris(2-carboxyethyl) phosphine (TCEP)); (c) measuring PTP activity (e.g., catalytic dephosphorylation activity), for example either continuously or at a fixed time point after addition of the reducing agent; and (d) comparing the rate of appearance of PTP activity in the presence of the candidate agent to that measured in the absence of the candidate agent. By using such methods of the invention, it is now possible to determine whether such candidate agents are binding to the oxidized PTP (PTP-SN) and slowing, hindering, impairing, inhibiting, or preventing the reappearance of PTP activity (thereby providing means for modulating or altering PTP activity).

Alternatively, a representative assay comprises the following steps: (a) contacting a biological sample comprising a cell containing the desired PTP with a reactive oxygen species or other means for causing the PTP to be oxidized into the PTP-SN state; (b) contacting (combining, mixing, adding together or otherwise introducing a

PTP-SN to a test compound to form a composition) the PTP-SN containing cell with a candidate agent, for example, a test compound that is a small organic molecule, (c) adding a reducing agent to the agent:PTP-SN composition (the composition being a mixture of the agent and PTP-SN in which a portion of or all of the agent present in the mixture may form a complex with a portion or all of the PTP-SN); non-limiting examples of reducing agents include the thiol-containing compounds such as beta-mercaptoethanol, dithiothreitol (DTT), dithioerythritol (DTE) or glutathione, or non-thiol reducing agents such as phosphines (*e.g.*, tris(2-carboxyethyl) phosphine (TCEP)); (d) measuring PTP activity (*e.g.*, dephosphorylation catalytic activity), for example either continuously or at a fixed time point after addition of the reducing agent; and (e) comparing the rate of appearance of PTP activity in the presence of the candidate agent to that measured in the absence of the candidate agent. By using such methods of the invention, it is now possible to determine whether such candidate agents are binding to the oxidized PTP (PTP-SN) and slowing, hindering, inhibiting, or preventing the reappearance of PTP activity (thereby providing means for modulating or altering PTP activity).

A "biological sample" as used herein refers to a sample containing at least one protein tyrosine phosphatase, and may be provided by obtaining a blood sample, biopsy specimen, tissue explant, organ culture, or any other tissue or cell preparation from a subject or a biological source. A sample may further refer to a tissue or cell preparation in which the morphological integrity or physical state has been disrupted, for example, by dissection, dissociation, solubilization, fractionation, homogenization, biochemical or chemical extraction, pulverization, lyophilization, sonication or any other means for processing a sample derived from a subject or biological source.

The subject or biological source may be a human or non-human animal, a primary cell culture, or culture adapted cell line including but not limited to genetically engineered cell lines that may contain chromosomally integrated or episomal recombinant nucleic acid sequences, immortalized or immortalizable cell lines, somatic cell hybrid cell lines, differentiated or differentiable cell lines, transformed cell lines and the like. Optionally, in certain situations it may be desirable to treat cells in a biological sample

with hydrogen peroxide and/or with another agent that directly or indirectly promotes reactive oxygen species (ROS) generation, including biological stimuli as described herein. In certain other situations it may be desirable to treat cells in a biological sample with a ROS scavenger, such as N-acetyl cysteine (NAC) or superoxide dismutase (SOD) or other ROS scavengers known in the art. In other situations cellular glutathione (GSH) may be depleted by treating cells with L-buthionine-SR-sulfoximine (Bso), and in other circumstances cells may be treated with pervanadate to enrich the sample in tyrosine phosphorylated proteins. Other means may also be employed to effect an increase in the population of tyrosine phosphorylated proteins present in the sample, including the use of a subject or biological source that is a cell line that has been transfected with at least one gene encoding a protein tyrosine kinase.

Various means are available to those skilled in the art for measuring the regeneration of an active PTP following reduction of the PTP-SN form. By way of non-limiting example, it is conventionally possible to measure the restored accessibility of the catalytic site thiol by reaction with a thiol-specific agent. Such thiol-specific agents are well known in the art and include Iac, IAM, and 4-vinyl pyridine. Detection can be determined by use of a detectable label, such as radioactive label, fluorescent label, biotin label, or Deuterium followed by detection using a mass spectrometer.

In another embodiment, the assays and methods described herein may be used for determining whether an agent specifically binds to a double mutant protein tyrosine phosphatase (PTP) polypeptide, that is, the agent does not bind to the corresponding wildtype PTP. The method may comprise contacting a double mutant PTP as described herein with a candidate agent or test compound under conditions and for a time sufficient to permit interaction between the mutant PTP and the candidate agent, and also contacting the corresponding wildtype PTP polypeptide with the candidate agent under conditions and for a time sufficient to permit interaction between the wildtype PTP and the candidate agent. The level of binding of the candidate agent to the mutant PTP may then be determined according to methods described herein and compared with the level of binding of the candidate agent to the wildtype PTP. An increased level of

binding of the agent or compound to the mutant PTP relative to the level of binding to the wildtype PTP indicates that the agent specifically binds to the mutant PTP polypeptide. Similarly, an agent that alters reduction of a PTP-SN may be identified by contacting, combining, or mixing, a candidate agent (or test compound) with a double mutant PTP and also combining the agent or compound with the corresponding wildtype PTP and comparing the level of binding of the agent or compound to each of the double mutant PTP and wildtype PTP. An increased or decreased level of binding of the agent to the mutant PTP indicates that the agent alters reduction of the corresponding PTP-SN.

An alternative representative assay comprises the steps of: (a) contacting a biological sample comprising a cell, such cell being capable of expressing the PTP, with a reactive oxygen species or other means for oxidizing the catalytic cysteine of the PTP to create a PTP-SN form; (b) contacting (combining, mixing, adding together, or otherwise introducing a biological sample to a test compound to form a composition) the biological sample or cell with a candidate agent such as, for example, a test compound that is a small organic molecule; (c) and measuring the binding of agent to protein. Step (c) can be accomplished by any of many described and conventional methods, including but not limited to thermal shift measurements, a technique that compares the thermal melting temperature shift of a free, unbound molecule compared to that of a molecule bound by an agent.

In a related embodiment, the assay may comprise a functional readout (*e.g.*, assessment of phosphoprotein phosphorylation state) to monitor whether the agent that binds to the PTP-SN also prevents restoration of PTP catalytic activity, for example, by observing persistent phosphorylation (*e.g.*, of a tyrosine residue) in a phosphorylated substrate using standard techniques. In another related embodiment, the assay may comprise a binding readout (*e.g.*, assessment of substrate binding by a substrate trapping mutant PTP) to monitor whether the agent that binds to the PTP-SN form of a substrate trapping mutant PTP also prevents restoration of substrate binding capability following exposure to a reducing agent, for example, using means for determining binding of a

suitable PTP substrate to the substrate trapping mutant PTP, such as those described herein and known to the art.

In another representative binding assay, a PTP-SN is produced or made in a substantially purified or substantially isolated form, or preferably in an isolated or
5 purified form, using methods described herein or through other means that comprise controlled oxidation of the catalytic cysteine. The assay comprises the steps of (a) contacting the PTP-SN with a candidate agent such as, for example, a small organic molecule; (b) and measuring the binding of agent to protein.

Step (b) can be accomplished by any of many described and conventional
10 methods, including but not limited to thermal shift measurements, a technique that compares the thermal melting temperature shift of a free unbound molecule compared to that of a molecule bound by an agent. Companies that have developed such thermal-shift technologies include Anadys Pharmaceuticals, San Diego, Calif., and 3D Pharmaceuticals (a Johnson and Johnson subsidiary) (*See also, e.g.,* Pantoliano et al., *J. Biomol. Screen.*
15 6:429-40 (2001)). Other variations for step (b) include measurement of mass changes, such as by detection using a mass spectrometer. Still other methods for measuring binding of agent to protein comprised in step (b) above include site-directed ligand discovery as discussed in the art by Erlanson, et al. (2000) *Proc. Natl. Acad. Sci. USA* 97:9367-937, and Arkin et al., *Proc. Natl. Acad. Sci. USA* 100: 1603-1608, each of which
20 is incorporated herein by reference. In other embodiments, binding of a candidate compound to a PTP-SN, and/or to a double mutant PTP that conformationally mimics a PTP-SN as described herein, may be determined according to the methods described herein using nuclear magnetic resonance (NMR) (Fejzo et al., *supra*; Hajduk et al., *supra*; van Dongen et al., *supra*) or crystallography methods adapted for high throughput
25 screening (Blundell et al., (2002), *supra*; Carr et al., *supra*; Stewart et al., *supra*; Rowland, *supra*).

In another embodiment, a method for identifying a compound that binds to a PTP-SN comprises contacting a PTP-SN with a test compound and determining binding of the compound to the PTP-SN by using an X-ray crystallography method. An isolated PTP-

SN may be crystallized according to methods described herein and known in the art. The step of contact a PTP-SN with a test compound when using an X-ray crystallography technique is understood to mean that the compound is soaked or incubated with the crystal in a solution containing the candidate compound. Binding of the compound to the PTP-SN
5 may then be determined according to X-ray crystallography methods described herein and known in the art, for instance, by electron density mapping (*see, e.g.*, Johnson and Blundell, *Protein Crystallography* (Academic Press 1976); Blundell et al. *Nat. Rev. Drug Discov.* 1:45-54 (2002)).

In other embodiments, a method for determining whether a compound binds
10 to a PTP-SN may include isothermal titration calorimetry in the solution state (Weber et al., *Curr. Opin. Struct. Biol.* 13:115-21 (2003); Ward et al., *Prog. Med. Chem.* 38:309-76 (2001); Cliff et al., *J. Mol. Recognit.* 16:383-91 (2003)); surface plasmon resonance (*e.g.*, BIAcore, Biosensor, Piscataway, NJ); or capillary electrophoresis (*see, e.g.*, Cetek, Inc.).

15 ANTIBODIES

Also contemplated by the present invention are binding molecules that are peptides, polypeptides, and other non-peptide molecules that specifically bind to a PTP-SN and that specifically bind to a double mutant of the corresponding PTP as described herein. Such binding molecules can be used in a process for purifying the PTP-SN or the
20 double mutant PTP, used for a therapy for treating a disease or condition associated with the PTP, or used in a diagnostic assay. As used herein, a molecule is said to specifically bind to a particular PTP-SN or to the particular double mutant PTP if it reacts at a detectable level with the PTP-SN and the double mutant PTP but does not react detectably with peptides containing an unrelated sequence or with a different
25 phosphatase. Preferred binding molecules include antibodies, which may be, for example, polyclonal, monoclonal, single chain, chimeric, humanized, anti-idiotypic, or CDR-grafted immunoglobulins, or antigen-binding fragments thereof, such as proteolytically generated or recombinantly produced immunoglobulin F(ab')₂, Fab, Fab', Fv, and Fd fragments. An antibody according to the present invention may belong to any

immunoglobulin class, for example IgG, IgE, IgM, IgD, or IgA. It may be obtained from or derived from an animal, for example, fowl (*e.g.*, chicken) or a mammal, which includes but is not limited to a mouse, rat, hamster, rabbit, or other rodent, a cow, horse, sheep, goat, camel, human, or other primate. The antibody may be an internalising antibody, or the
5 antibody may be modified so that it may be easily transported across a cell membrane.

Certain preferred antibodies are those antibodies that inhibit, hinder, or block PTP-SN from being reactivated to a catalytically active PTP; such antibodies also specifically bind to a double mutant of the corresponding PTP as described herein. Binding properties of an antibody to PTP-SN and to the double mutant of the
10 corresponding PTP may generally be assessed using conventional immunodetection methods including, for example, an enzyme-linked immunosorbent assay (ELISA), immunoprecipitation, radioimmunoassays, immunoblotting and the like, which may be readily performed by those having ordinary skill in the art. A skilled artisan will also be familiar with such immunodetection methods that when used to detect an antibody that
15 binds to a conformational epitope of a polypeptide, the method may require that any reagent or condition which could potentially denature the polypeptide and thus alter or destroy the conformational epitope be avoided or minimized.

In one embodiment, the antibody or antigen binding fragment thereof binds to an epitope that includes the catalytic cysteine residue in the sulphenyl-amide
20 form. The epitope may comprise amino acid residues that are present in a contiguous segment of the sequence and that includes the catalytic cysteine. In another embodiment, the antibody or antigen binding fragment thereof binds to a conformational epitope that is formed in a sulphenyl-amide species of the PTP. In another embodiment, the antibody or antigen-binding fragment thereof binds to a double mutant PTP that has a substitution of
25 the catalytic cysteine residue and a substitution of the adjacent C-terminal residue (*e.g.*, in a classical PTP, a substitution of cysteine with alanine and a substitution of the serine residue with an alanine residue). Such an antibody would also specifically bind to the PTP in the PTP-SN form. In a particular embodiment, the antibody or antigen binding fragment thereof recognizes a conformational epitope that results from conformational

changes that occur in the double mutant PTP as a result of the amino acid substitutions, and which conformational epitope is not present in the corresponding wildtype PTP.

Methods well known in the art and described herein may be used to generate antibodies, including polyclonal antisera or monoclonal antibodies, that are specific for a PTP-SN or a double mutant PTP. Antibodies also may be produced as genetically engineered immunoglobulins (Ig) or Ig fragments designed to have desirable properties. For example, by way of illustration and not limitation, antibodies may include a recombinant IgG that is a chimeric fusion protein having at least one variable (V) region domain from a first mammalian species and at least one constant region domain from a second, distinct mammalian species (*see, e.g., Morrison et al., Proc. Natl. Acad. Sci. USA*, 81:6851-55 (1984); Shin et al., *Methods Enzymol.* 178:459-76 (1989); Walls et al., *Nucleic Acids Res.* 21:2921-29 (1993); U.S. Patent No. 5,482,856). Most commonly, a chimeric antibody has murine variable region sequences and human constant region sequences. Such a murine/human chimeric immunoglobulin may be "humanized" by grafting the complementarity determining regions (CDRs) derived from a murine antibody, which confer binding specificity for an antigen, into human-derived V region framework regions and human-derived constant regions (*see, e.g., Jones et al., Nature* 321:522-25 (1986); Riechmann et al., *Nature* 332:323-27 (1988); Padlan et al., *FASEB* 9:133-39 (1995); Chothia et al., *Nature*, 342:377-383 (1989); Bajorath et al., *Ther. Immunol.* 2:95-103 (1995); EP-0578515-A3). Fragments of these molecules may be generated by proteolytic digestion, or optionally, by proteolytic digestion followed by mild reduction of disulfide bonds and alkylation. Alternatively, such fragments may also be generated by recombinant genetic engineering techniques.

An antibody that is immunospecific or that specifically binds to a PTP-SN polypeptide, PTP-SS, and/or a double mutant PTP as provided herein reacts at a detectable level with PTP-SN, PTP-SS, and/or a double mutant PTP and not with unrelated polypeptides, preferably with an affinity constant, K_a , of greater than or equal to about 10^4 M^{-1} , more preferably of greater than or equal to about 10^5 M^{-1} , more preferably of greater than or equal to about 10^6 M^{-1} , and still more preferably of greater

than or equal to about 10^7 M⁻¹. Affinity of an antibody for its cognate antigen is also commonly expressed as a dissociation constant K_D , and an anti-PTP (or PTP-SN, PTP-SS, or double mutant PTP) antibody specifically binds to the PTP if it binds with a K_D of less than or equal to 10^{-4} M, less than or equal to about 10^{-5} M, less than or equal to about
5 10^{-6} M, less than or equal to 10^{-7} M, or less than or equal to 10^{-8} M. Affinities of binding partners or antibodies can be readily determined using conventional techniques, for example, those described by Scatchard et al. (*Ann. N.Y. Acad. Sci. USA* 51:660 (1949)) or by surface plasmon resonance (BIAcore, Biosensor, Piscataway, NJ). See, e.g., Wolff et al., *Cancer Res.* 53:2560-2565 (1993).

10 Antibodies may generally be prepared by any of a variety of techniques known to those skilled in the art. See, e.g., Harlow et al., *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory (1988). In one such technique, an animal is immunized with the immunogen PTP-SN or a double mutant PTP, or a fragment or peptide thereof, as an antigen to generate polyclonal antisera. Suitable animals include,
15 for example, rabbits, sheep, goats, pigs, cattle, and may also include smaller mammalian species, such as mice, rats, and hamsters, or other species.

 An immunogen may be comprised of cells expressing PTP-SN, PTP-SS, or double mutant PTP, purified or partially purified PTP-SN, PTP-SS, or double mutant PTP, polypeptides, or variants or fragments (e.g., a fragment comprising the PTP catalytic
20 domain or a portion thereof) thereof, or PTP-SN peptides. PTP-SN peptides may be generated by proteolytic cleavage or may be chemically synthesized. Similarly, immunogens that may be used to generate antibodies that specifically bind to the double mutant PTP may be comprised of cells expressing the double mutant PTP, purified or partially purified double mutant PTP polypeptides, or variants or fragments (e.g., a
25 fragment comprising the catalytic domain) or peptides thereof. Fragments and/or peptides may be generated by proteolytic cleavage or may be chemically synthesized. For instance, nucleic acid sequences encoding PTP-SN polypeptides and double mutant PTPs polypeptides are provided herein, such that those skilled in the art may routinely prepare these polypeptides for use as immunogens. Peptides may be chemically synthesized by

methods as described herein and known in the art. Alternatively, peptides may be generated by proteolytic cleavage of a PTP-SN polypeptide, and individual peptides isolated by methods known in the art such as polyacrylamide gel electrophoresis or any number of liquid chromatography or other separation methods.

5 Peptides useful as immunogens typically may have an amino acid sequence of at least 4 or 5 consecutive amino acids from a PTP-SN or PTP-SS amino acid sequence or a double mutant PTP amino acid sequence such as those described herein, and preferably have at least 6, 7, 8, 9, 10, 11, 12, 14, 15, 16, 18, 19 or 20 consecutive amino acids of a PTP-SN or PTP-SS polypeptide or a double mutant PTP
10 polypeptide. Certain other preferred peptide immunogens may comprise 21-25, 26-30, 31-35, 36-40, 41-50 or more consecutive amino acids of a PTP-SN or PTP-SS polypeptide sequence or a double mutant PTP polypeptide sequence. Polypeptides or peptides useful for immunization may also be selected by analyzing the primary, secondary, and tertiary structure of PTP-SN or a double mutant PTP polypeptide
15 according to methods known to those skilled in the art, in order to determine amino acid sequences more likely to generate an antigenic response in a host animal. *See, e.g.,* Novotny, 1991 *Mol. Immunol.* 28:201-207; Berzofsky, 1985 *Science* 229:932-40; Chang et al. *J. Biochem.* 117:863-68 (1995); Kolaskar et al. *Viology* 261:31-42 (1999)). Such polypeptide fragment or peptide may comprise the signature catalytic cysteine motif (SEQ
20 ID NO:1) or any of SEQ ID NOS:2-21, 106, 107, and 109. Preferably, the polypeptide or peptide comprises a sufficient number of amino acids to fold in a manner that approximates the conformation of the catalytic domain in a full-length PTP-SN or PTP-SS or double mutant PTP polypeptide.

Immunogens may be prepared and animals immunized according to
25 methods well known in the art. *See, e.g.,* Harlow et al., *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory (1988). The immune response may be monitored by periodically bleeding the animal, separating the sera out of the collected blood, and analyzing the sera in an immunoassay, such as an ELISA or Ouchterlony diffusion assay, or the like, to determine the specific antibody titer. Once an antibody

titer is established, the animals may be bled periodically to accumulate the polyclonal antisera. Polyclonal antibodies that bind specifically to the PTP-SN or PTP-SS polypeptide or peptide (or to the double mutant PTP polypeptide or peptide) may then be purified from such antisera, for example, by affinity chromatography using protein A, an antibody that specifically binds to a constant region (heavy or light chain) of the antibody(ies) to be purified, or the PTP-SN polypeptide (or the double mutant PTP polypeptide), immobilized on a suitable solid support.

Monoclonal antibodies that specifically bind to PTP-SN or to PTP-SS polypeptides or fragments or variants thereof, (or to double mutant PTP polypeptides or fragments or variants thereof) and hybridomas, which are immortal eukaryotic cell lines, that produce monoclonal antibodies having the desired binding specificity, may also be prepared, for example, using the technique of Kohler and Milstein (*Nature*, 256:495-497; 1976, *Eur. J. Immunol.* 6:511-519 (1975)) and improvements thereto with which a skilled artisan is familiar. An animal—for example, a rat, hamster, or a mouse—is immunized with a PTP-SN or PTP-SN immunogen, lymphoid cells that include antibody-forming cells, typically spleen cells, are obtained from the immunized animal and may be immortalized by fusion with a drug-sensitized myeloma (e.g., plasmacytoma) cell fusion partner.

Monoclonal antibodies may be isolated from the supernatants of hybridoma cultures or isolated from a mouse that has been treated (e.g., pristane-primed) to promote formation of ascites fluid containing the monoclonal antibody. Antibodies may be purified by affinity chromatography using an appropriate ligand selected based on particular properties of the monoclonal antibody (e.g., heavy or light chain isotype, binding specificity, etc.). Examples of a suitable ligand, immobilized on a solid support, include Protein A, Protein G, an anti-constant region (light chain or heavy chain) antibody, an anti-idiotypic antibody and a PTP-SN or PTP-SN polypeptide or fragment or variant thereof (or to a double mutant PTP polypeptide or fragment or variant thereof).

Human monoclonal antibodies may be generated by any number of techniques with which those having ordinary skill in the art will be familiar. Antibodies

may also be identified and isolated from human immunoglobulin phage libraries, from rabbit immunoglobulin phage libraries, and/or from chicken immunoglobulin phage libraries (see, e.g., Winter et al., 1994 *Annu. Rev. Immunol.* 12:433-55; Burton et al., 1994 *Adv. Immunol.* 57:191-280; U.S. Patent No. 5,223,409; Huse et al., 1989 *Science* 246:1275-81; Schlebusch et al., 1997 *Hybridoma* 16:47-52 and references cited therein; Rader et al., *J. Biol. Chem.* 275:13668-76 (2000); Popkov et al., *J. Mol. Biol.* 325:325-35 (2003); Andris-Widhopf et al., *J. Immunol. Methods* 242:159-31 (2000)). Antibodies isolated from non-human species or non-human immunoglobulin libraries may be genetically engineered according to methods described herein and known in the art to "humanize" the antibody or fragment thereof.

In certain embodiments, a B cell from an immunized animal that is producing an anti-PTP-SN, PTP-SN, or an anti-mutant PTP, including an anti-double mutant PTP, antibody is selected and the light chain and heavy chain variable regions are cloned from the B cell according to molecular biology techniques known in the art (WO 92/02551; US patent 5,627,052; Babcook et al., *Proc. Natl. Acad. Sci. USA* 93:7843-48 (1996)) and described herein. Preferably B cells from an immunized animal are isolated from the spleen, lymph node, or peripheral blood sample by selecting a cell that is producing an antibody that specifically binds to PTP-SN or to a double mutant PTP. B cells may also be isolated from humans, for example, from a peripheral blood sample.

An antibody fragment may also be any synthetic or genetically engineered protein that acts like an antibody in that it binds to a specific antigen to form a complex. For example, antibody fragments include isolated fragments consisting of the light chain variable region; "Fv" fragments consisting of the variable regions of the heavy and light chains; recombinant single chain polypeptide molecules in which light and heavy variable regions are connected by a peptide linker (scFv proteins); and minimal recognition units consisting of the amino acid residues that mimic the hypervariable region. Such an antibody fragment preferably comprises at least one variable region domain. (see, e.g., Bird et al., *Science* 242:423-26 (1988); Huston et al., *Proc. Natl. Acad. Sci. USA* 85:5879-5883

(1988); EP-B1-0318554; U.S. Patent No. 5,132,405; U.S. Patent No. 5,091,513; and U.S. Patent No. 5,476,786).

In certain embodiments, an antibody that specifically binds to a PTP-SN or to a double mutant PTP may be an antibody that is expressed as an intracellular protein.

5 Such intracellular antibodies are also referred to as intrabodies and may comprise an Fab fragment, or preferably comprise a scFv fragment (*see, e.g., Lecerf et al., Proc. Natl. Acad. Sci. USA* 98:4764-49 (2001)). The framework regions flanking the CDR regions can be modified to improve expression levels and solubility of an intrabody in an intracellular reducing environment (*see, e.g., Worn et al., J. Biol. Chem.* 275:2795-803

10 (2000)). An intrabody may be directed to a particular cellular location or organelle, for example by constructing a vector that comprises a polynucleotide sequence encoding the variable regions of an intrabody that may be operatively fused to a polynucleotide sequence that encodes a particular target antigen within the cell (*see, e.g., Graus-Porta et al., Mol. Cell Biol.* 15:1182-91 (1995); Lener et al., *Eur. J. Biochem.* 267:1196-205

15 (2000)). An intrabody may be introduced into a cell by a variety of techniques available to the skilled artisan including via a gene therapy vector, or a lipid mixture (*e.g., Provectin™* manufactured by Imgenex Corporation, San Diego, CA), or according to photochemical internalization methods.

The polynucleotides encoding an antibody or fragment thereof that

20 specifically bind a PTP-SN, PTP-SS, or double mutant PTP, as described herein, may be propagated and expressed according to any of a variety of well-known procedures for nucleic acid excision, ligation, transformation, and transfection using any number of known expression vectors. Thus, in certain embodiments expression of an antibody fragment may be preferred in a prokaryotic host, such as *Escherichia coli* (*see, e.g.,*

25 Pluckthun et al., 1989 *Methods Enzymol.* 178:497-515). In certain other embodiments, expression of the antibody or a fragment thereof may be in a eukaryotic host cell, including yeast (*e.g., Saccharomyces cerevisiae, Schizosaccharomyces pombe, and Pichia pastoris*), animal cells (including mammalian cells) or plant cells. Examples of suitable

animal cells include, but are not limited to, myeloma, COS, CHO, or hybridoma cells. Examples of plant cells include tobacco, corn, soybean, and rice cells.

Antibodies that specifically bind to a PTP-SN and the corresponding double mutant PTP may be used in assays described herein for screening of candidate or test
5 compounds that promote the cyclic sulfenyl-amide form of the PTP. In another embodiment, such antibodies that specifically bind to the PTP-SN may be used in screening assays to identify compounds that shift the active PTP:inactive PTP-SN equilibrium toward the inactive PTP-SN form.

In certain preferred embodiments, an antibody or antigen binding fragment
10 thereof that specifically binds to a PTP-SN or PTP-SS may be delivered to the interior of a cell as an intact polypeptide. For example, methods to deliver exogenous proteins intracellularly may include the use of protein transduction domains as peptide carriers, for example, HIV-1 TAT, *Drosophila* Antennapedia homeotic transcription factor, and herpes simplex virus-1 DNA binding protein VP22 (Schwarze et al., *Trends Cell Biol.*
15 10:290-95 (2000)). To intracellularly deliver an active protein, correct renaturation of the antibody or antigen-binding fragment thereof is required upon internalization of the protein by the cell. Such delivery systems may require that the antibody be covalently linked to the delivery molecule and/or chemical modification of the polypeptide. Another delivery system provides an amphipathic peptide carrier that can form a non-covalent
20 complex with the antibody or antigen binding fragment thereof to be delivered to the cell (see Chariot™, Active Motif®, Carlsbad, CA; Morris et al., *J. Biol. Chem.* 274:24941-46 1999); Morris et al., *Nature Biotechnol.* 19:1173-76 (2110)). In another embodiment, the antibody or an antigen binding fragment thereof may be site-specifically attached to a peptide that comprises a membrane transport sequence that facilitates transport across
25 membranes (see, e.g., Zhao et al., *J. Immunol. Methods* 254:137-45 (2001); see also, e.g., InNexus Biotechnology Inc. (Vancouver, BC, Canada)).

THERAPEUTIC METHODS

One or more antibodies or agents identified according to the above-described methods may also be used to modulate (*e.g.*, inhibit or potentiate) target polypeptide activity in a patient. As used herein, a "patient" may be any mammal, including a human, and may be afflicted with a condition associated with undesired target polypeptide activity or may be free of detectable disease. Accordingly, the treatment may be of an existing disease or may be prophylactic. Conditions associated with signal transduction and/or with inappropriate activity of specific PTP polypeptides described herein include obesity, impaired glucose tolerance and diabetes and cancer, disorders associated with cell proliferation, including cancer, graft-versus-host disease (GVHD), autoimmune diseases, allergy or other conditions in which immunosuppression may be involved, metabolic diseases, abnormal cell growth or proliferation, and cell cycle abnormalities.

For administration to a patient, one or more antibodies or agents are generally formulated as a pharmaceutical composition. A pharmaceutical composition may be a sterile aqueous or non-aqueous solution, suspension or emulsion, which additionally comprises a physiologically acceptable carrier (*i.e.*, a non-toxic material that does not interfere with the activity of the active ingredient). Such compositions may be in the form of a solid, liquid or gas (aerosol). Alternatively, compositions of the present invention may be formulated as a lyophilizate or compounds may be encapsulated within liposomes using well known technology. Pharmaceutical compositions within the scope of the present invention may also contain other components, which may be biologically active or inactive. Such components include, but are not limited to, buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, stabilizers, dyes, flavoring agents, and suspending agents and/or preservatives.

Any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of the present invention. Carriers for

therapeutic use are well known, and are described, for example, in *Remingtons Pharmaceutical Sciences*, Mack Publishing Co. (A.R. Gennaro ed. 1985). In general, the type of carrier is selected based on the mode of administration. For example, a pharmaceutical composition (*e.g.*, for oral administration or delivery by injection) may be
5 in the form of a liquid (*e.g.*, an elixir, syrup, solution, emulsion or suspension). A liquid pharmaceutical composition may include, for example, one or more of the following: sterile diluents such as water for injection, saline solution, preferably physiological saline, Ringer's solution, isotonic sodium chloride, fixed oils such as synthetic mono or diglycerides which may serve as the solvent or suspending medium, polyethylene glycols,
10 glycerin, propylene glycol or other solvents; antibacterial agents such as benzyl alcohol or methyl paraben; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. A parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose
15 vials made of glass or plastic. The use of physiological saline is preferred, and an injectable pharmaceutical composition is preferably sterile.

The compositions described herein may be formulated for sustained release (*i.e.*, a formulation such as a capsule or sponge that effects a slow release of compound following administration). Such compositions may generally be prepared
20 using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain an agent dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the
25 formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Within a pharmaceutical composition, a therapeutic agent may be linked to any of a variety of compounds. For example, such an agent may be linked to a targeting moiety (*e.g.*, a monoclonal or polyclonal antibody, a protein or a liposome) that facilitates the delivery of the agent to the target site. As used herein, a "targeting moiety" may be any substance (such as a compound or cell) that, when linked to an agent enhances the transport of the agent to a target cell or tissue, thereby increasing the local concentration of the agent. Targeting moieties include antibodies or fragments thereof, receptors, ligands, and other molecules that bind to cells of, or in the vicinity of, the target tissue. An antibody targeting agent may be an intact (whole) molecule, a fragment thereof, or a functional equivalent thereof. Linkage is generally covalent and may be achieved by, for example, direct condensation or other reactions, or by way of bi- or multi-functional linkers. Targeting moieties may be selected based on the cell(s) or tissue(s) toward which the agent is expected to exert a therapeutic benefit.

Pharmaceutical compositions may be administered in a manner appropriate to the disease to be treated (or prevented). An appropriate dosage and a suitable duration and frequency of administration will be determined by such factors as the condition of the patient, the type and severity of the patient's disease, the particular form of the active ingredient and the method of administration. In general, an appropriate dosage and treatment regimen provides the agent(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit (*e.g.*, an improved clinical outcome, such as more frequent complete or partial remissions, or longer disease-free and/or overall survival, or a lessening of symptom severity). For prophylactic use, a dose should be sufficient to prevent, delay the onset of, or diminish the severity of a disease associated with cell proliferation.

Optimal doses may generally be determined using experimental models and/or clinical trials. In general, the amount of PTP-specific agent or antibody in a dose ranges from about 0.01 μg to about 100 μg per kg of host weight, typically from about 0.1 μg to about 10 μg . The minimum dose that is sufficient to provide effective therapy is usually preferred. Patients may generally be monitored for therapeutic or prophylactic

effectiveness using assays suitable for the condition being treated or prevented, which will be familiar to those having ordinary skill in the art. Suitable dose sizes will vary with the size, age, and/or mass of the patient, but will typically range from about 10 ml to about 500 ml for a 10-60 kg subject.

5

The following Examples are offered by way of illustration and not by way of limitation.

EXAMPLE 1

OXIDATION AND REDUCTION OF PTP1B

10

Crystals of PTP1B oxidized in solution followed by crystallization.

Purified PTP1B (Barford et al. (1994), *supra*) was dialyzed into DTT free buffer A (10 mM Tris pH 7.5, 25 mM NaCl, 0.2 mM EDTA). After dialysis, the protein concentration was 32 μ M, and 40 μ M H₂O₂ was added (ratio of 1:1.25). The protein was oxidized for 15 50 min at room temperature (RT) and concentrated to 8.5 mg/ml and crystallized (*id.*) without DTT. Data were collected on crystals at 3 weeks and 3 months after the protein was put into crystallization trials. The structures were solved as described for the time course of oxidation (see below).

Crystallization followed by oxidation. The catalytic domain of PTP1B 20 (residues 1-321) was purified and crystallized at 4 °C (*id.*). To oxidize the protein, crystals were first washed for 1-2 minutes in 40 μ l of crystallization well solution (0.1 M Hepes, pH 7.5, 0.2 M MgOAc, 0.2 mM EDTA, and PEG ranging from 12-17%) to remove the DTT. The crystals were then transferred to 40 μ l of crystallization well solution plus 50 μ M H₂O₂. They were soaked for time periods ranging from 20 min to 16 25 h (*see* Table 1) before being frozen in cryoprotectant buffer (0.1 M Hepes pH 7.5, 0.2 M MgOAc, 0.2 mM EDTA, 17.5% methyl-pentane diol, and PEG ranging from 18-20%). Data were collected at Chester Beatty Laboratories (London, UK), Synchrotron Radiation Source (SRS, Daresbury, UK), or the European Synchrotron Radiation Facility (ESRF, Grenoble, France) and were processed using the HKL package, (Table 1, Figures 8 and 9)

(Otwinowski et al., *Methods in Enzymol.* 276:307-26 (1997)). The resolution ranged from 2.3-1.7 Å. Since the crystals were isomorphous with wild type PTP1B, its structure was used as a starting model for refinement (Barford et al. (1994), *supra*) using CNS (Brunger et al., *Acta Crystallalog.* D54:905-21 (1998)). Monomer libraries for the
5 sulfenic acid and sulfenyl-amide states of the catalytic cysteine were built using REFMAC as part of the CCP4gui (Collaborative Computational Project No. 4, *Acta Crystallogr. D* 50:670-63 (1994)). Final structures were obtained by an additional one to two rounds of refinement in REFMAC using the appropriate monomer libraries. After a model of the oxidized protein was built, this model was used as the starting model when it resulted in a
10 lower R-factor after the initial rounds of refinement. Final R_{factors} ranged from 18-21% and final R_{free} values of 22 to 23% (Table 1 below).

Table 1a. Crystallographic Data Collection and Refinement Statistics for Oxidation Time Course in 50 μ M H₂O₂

Length of oxidation (min)	0 min	40 min	75 min	2 hour	5 hour	16 hour
Oxidation state of Cys215 ¹	S ⁻	75% S ⁻ /25% SN	50% S ⁻ /50% SN	SN	SN	SO ₂ /SO ₃
PTP loop	Closed	Closed/open	Closed/open	Open	Open	Closed
pTyr loop	Closed	Closed/open	Closed/open	Open	Open	Closed
Space group (Z)	P3 ₁ 21	P3 ₁ 21	P3 ₁ 21	P3 ₁ 21	P3 ₁ 21	P3 ₁ 21
Unit Cell Parameters						
a, b (Å)	88.593	88.478	88.349	88.379	88.291	88.701
c (Å)	104.982	104.468	104.186	104.155	104.110	104.688
Z	1	1	1	1	1	1
X-ray source	In-house	In-house	id14eh1	SRS 9.6	SRS 9.6	SRS 9.6
λ (Å)	1.541	1.541	0.933	1.004	1.004	1.004
Resolution (Å)	25.0-2.10	25.00-2.15	50.0-1.7	50.0-1.90	50.0-1.95	50.0-2.0
Observations (N)	172,491	207,986	276,849	491,640	387,847	454,203
Unique (N)	28,289	26,116	51,760	37,560	31,895	32,529
Completeness (%) ²	99.9 (99.7)	99.6%	99.1%	99.9	98.9 (98.0)	99.3 (97.9)
R _{sym} ^{2,3}	0.066 (0.378)	0.066 (0.41)	0.053 (.386)	0.040 (0.421)	0.048 (0.303)	0.073 (0.256)
I/ σ I ²	22.62 (3.33)	26.38 (2.84)	24.00 (1.73)	49.8 (4.70)	46.5 (5.80)	35.88 (4.82)
Refinement						
Resolution range (Å)	76.70-2.10	23.00-2.15	76.70-1.80	43.03-1.90	43.03-1.95	31.78-2.00
Reflections working set	26,846	24,789	41,756	35,694	32,600	30,880
R _{free} set (N) (%)	1443 (5.1%)	1324 (5.1%)	2241 (5.1%)	1922 (5.1%)	1748 (5.1%)	1649 (5.1%)
R _{crys} ^{2,4} /R _{free} ^{2,5}	0.1976/0.2172	0.180/0.222	0.181/0.201	0.213/0.236	0.206/0.231	0.207/0.235
Protein atoms (N)	2289	2289	2289	2289	2289	2290
Solvent atoms (N)	163	140	178	145	154	133
Rmsd bond angles (°)	1.877	2.072	1.663	1.818	1.869	1.932
Rmsd bond lengths (Å)	0.026	0.029	0.019	0.023	0.024	0.028

**Table1b: Data for Oxidation of PTP1B Using
Equimolar H₂O₂ Prior to Crystallization**

Time until data-collection	3-week	3-month
Oxidation state of Cys215 ¹	SN	SO ₃
PTP loop	Open	Closed
pTyr loop	Open	Closed
Space group (Z)	P3 ₁ 21	P3 ₁ 21
Unit Cell Parameters		
a,b (Å)	88.218	88.368
c (Å)	103.787	104.783
Z	1	1
X-ray source	id14eh1	In-house
λ (Å)	0.933	1.541
Resolution (Å)	50-1.75	50.0-2.40
Observations (N)	308,523	137,296
Unique (N)	43,606	18,467
Completeness (%) ²	99.5 (99.3)	97.2 (95.9)
$R_{\text{sym}}^{2,3}$	0.039 (0.355)	0.086 (0.366)
$I/\sigma I^2$	26.26 (2.68)	19.79 (3.84)
Refinement		
Resolution range (Å) rfm	76.70-1.80	76.70-2.40
Reflections working set rfm	41389	17,535
R_{free} set (N) (%)	2217 (5.1%)	932 (5.0%)
$R_{\text{cryst}}^{2,4}/R_{\text{free}}^{2,5}$ (rfm)	0.204/0.226	0.181/0.227
Protein atoms (N)	2289	2291
Solvent atoms (N)	181	142
Rmsd bond angles (°) rfm	1.785	2.164
Rmsd bond lengths (Å) rfm	0.0200	0.033

Table 1c. Data for Sulfenyl-Amide Reduction Experiment Using DTT or GSH

Length of Oxidation	~12 hours	~12 hours	~16 hours	~16 hours
Length of Reduction/ Reducing agent	0 hours	72hours/5mM DTT	0 hours	72 hours/ 5mM GSH
Oxidation state of Cys215 ¹	SN	S ⁻	SN	S ⁻
PTP loop	Open	Closed	Open	Closed
pTyr loop	Open	Closed	Open	Closed
Space group (Z)	P3 ₁ 21	P3 ₁ 21	P3 ₁ 21	P3 ₁ 21
Unit Cell Parameters				
a,b (Å)	88.513	88.513	88.441	88.410
c (Å)	104.180	104.859	103.980	104.626
Z	1	1	1	1
X-ray source	In-house	In-house	In-house	id14eh1
λ (Å)	1.541	1.541	1.541	0.933
Resolution (Å)	25.0-2.2	25.0-2.3	25.0-2.3	50.0-1.90
Observations (N)	179,489	144,827	149,942	227,910
Unique (N)	24,440	21,540	21,226	37,661
Completeness (%) ²	99.5 (99.3)	99.7 (99.2)	99.1(98.4)	99.6 (98.0)
R _{sym} ^{2,3}	0.081 (0.447)	0.085 (0.423)	0.80 (0.47)	0.066 (0.176)
I/ σ I ²	19.36 (2.82)	19.10 (3.26)	17.13 (2.49)	26.56 (4.82)
Refinement				
Resolution range (Å)	76.70-2.20	76.70-2.30	76.70-2.30	76.70-1.90
Reflections working set	23204	20444	20144	35730
R _{free} set (N) (%)	1234 (5.0)	1096 (5.1%)	1082 (5.1%)	1931 (5.1%)
R _{cryst} ^{2,4} /R _{free} ^{2,5}	0.189/0.229	0.182/0.212	0.188/0.233	0.192/0.215
Protein atoms (N)	2289	2289	2289	2289
Solvent atoms (N)	134	132	121	197
Rmsd bond angles (°)	2.09	2.031	2.215	1.67
Rmsd bond lengths (Å)	0.029	0.028	0.031	0.021

Table 1d. Crystallographic Statistics for Pervanadate Soak and Co-Crystals with 130 μ M H_2O_2

Treatment	100 μ M pervanadate overnight soak	Co-crystals 130 μ M H_2O_2
Oxidation state of Cys215 ¹	SO ₃	SN
PTP loop	Closed	Open
pTyr loop	Closed	Open
Space group (Z)	P3 ₁ 21	P3 ₁ 21
Unit Cell Parameters		
a,b (Å)	88.365	88.322
c (Å)	104.764	104.076
Z	1	1
X-ray source	In-house	id14eh1
λ (Å)	1.541	0.933
Resolution (Å)	25.00-2.15	50.0-1.8
Observations (N)	183,671	236,569
Unique (N)		43,303
Completeness (%) ²	98.1 (96.7)	98.5 (97.5)
$R_{\text{sym}}^{2,3}$	0.071 (0.332)	0.053 (0.374)
$I/\sigma I^2$	25.68 (3.97)	22.57 (2.44)
Refinement		
Resolution range (Å)	76.70-2.15	76.70-1.80
Reflections working set	24,459	41,102
R_{free} set (N) (%)	1305 (5.1%)	2201 (5.1%)
$R_{\text{cryst}}^{2,4}/R_{\text{free}}^{2,5}$	0.185/0.215	0.201/0.223
Protein atoms (N)	2289	2289
Solvent atoms (N)	158	188
Rmsd bond angles (°)	1.894	1.689
Rmsd bond lengths (Å)	0.026	0.020

Table 1 footnotes:

¹For the oxidation states of the catalytic site cysteine: S⁻ = reduced cysteine, SN= the sulfenyl-amide bond between C215 and S216, SO₂= sulfinic acid, SO₃=sulfonic acid. The state used for generating the crystallographic statistics listed is highlighted in bold at the top of each table.

5 ²Numbers in parentheses refer to the values in the highest resolution shell.

³ $R_{\text{sym}} = \sum_h \sum_i |I(h) - I_i(h)| / \sum_h \sum_i I_i(h)$ where $I_i(h)$ and $I(h)$ are the i^{th} and mean measurements of the intensity of reflection h .

⁴ $R_{\text{cryst}} = \sum_{hkl} \|F_o\| - k \|F_c\| / \sum_{hkl} \|F_o\|$ where F_o and F_c are the observed and calculated structure factor amplitudes of reflection h , and k is a weighting factor.

$R_{\text{free}} = \sum_{hkl \in T} \|F_o\| - k \|F_c\| / \sum_{hkl} \|F_o\|$ where F_o and F_c are the observed and calculated structure factor amplitudes of reflection h , and k is a weighting factor. T is the test set of reflections.
 λ : wavelength, rmsd: root mean square deviation, Z : number of molecules in the asymmetric unit.

5 **Reduction of the sulfenyl-amide bond.** Crystals prepared as described for the time course were transferred into 4 μL of crystallization buffer with 20 μM H_2O_2 and soaked for 12 hours (prior to reduction with DTT) or 16 hours (prior to reduction with GSH). After the H_2O_2 soak, one crystal was frozen for data collection to verify that it was in the cyclic sulfenyl-amide state. The other three crystals were incubated in 40 μL
 10 of crystallization buffer with either DTT (5 mM) or GSH (5 mM) for 72 hours before data collection.

Crystals of PTP1B with pervanadate. Crystals were soaked in crystallization well solution without DTT and with 50 μM pervanadate. The pervanadate was a 1:1 ratio of sodium orthovanadate and H_2O_2 at room temperature for 20 min. The
 15 crystals were soaked ~14 hours.

Analysis of PTP1B in solution using mass spectrometry. PTP1B D181A and C215S mutant (56 μM) was incubated with the indicated concentrations of H_2O_2 for 10 minutes in 50 mM Hepes, pH 7.5, 1 mM EDTA, 200 μM DTT. One μL was digested with trypsin in 50 mM ammonium bicarbonate, pH 8.0, and analyzed using
 20 matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry. Ten μL were boiled for 10 minutes in SDS-loading buffer and analyzed by SDS-PAGE. To reversibly oxidize PTP1B (pulse-chase experiment), 30 μL 'heavy' $\text{H}_2^{18}\text{O}_2$ (2% stock solution, Icon 19 Ox Bow Lane, Summit, NJ) was added to an equal volume of 26 μM PTP1B in degassed buffer (50 mM Hepes, pH 7.5, 1 mM EDTA, 100
 25 μM DTT) giving final concentrations of between 5 and 5×10^4 μM . At 30 minutes, 10 μL of the PTP1B mixture were removed and chased with "light" $\text{H}_2^{16}\text{O}_2$ (>100 fold excess) for two hours and then trypsinized. Twenty μL were removed to assay enzyme activity (% inhibition) using 4-nitrophenyl phosphate (pNPP) as substrate. The remaining 30 μL of sample were incubated with DTT (10 mM) and catalase (10 units) for two hours, and the

recovered enzyme activity was measured using pNPP as substrate (% recovery). For trypsinolysis, PTP1B was diluted with 50 mM ammonium bicarbonate, pH 8.0, 5 mM DTT, and 0.3 µg of sequencing grade trypsin and incubated at 37 °C for 12-16 hours. One µL of digest was mixed with saturated α-cyano-4-hydroxycinnamic acid and
5 analyzed with a Voyager DE-RP mass spectrometer. Internal reference standards were used for calibration.

Oxidation induced disruption of PTP1B-IRK interactions. PTP1B D181A (12 µg) diluted in 50 mM Tris, pH 7.6, 0.1 mM DTT was oxidized with increasing concentrations of H₂O₂ at room temperature in a total volume of 400 µl. After
10 10 minutes of oxidation, kinase buffer (50 mM Tris pH 7.6, 4 mM MnCl₂, 10 mM MgCl₂, 100 µM ATP) containing purified autophosphorylated insulin receptor (IR, 2 µg) and γ-³²P-ATP was added to each sample (1 ml final volume). After 20 minutes, the kinase reaction was terminated by addition of EDTA, PTP1B was immunoprecipitated with FG6 antibody, and proteins in the immunocomplexes were resolved by SDS-PAGE.

15 Similar experimental methods may be carried out following the above-described materials and methods to create and test PTP-SN or PTP-SS forms of any PTP including, without limitation, the classical PTPs as described by Andersen et al. (2001) and Andersen et al. (2004); PTP-eta, PTP-epsilon, DEP-1 (CD148), SHP2, SHP1, cdc25 (a, b, or c), cdc14a, cdc14b, DSP-2, DSP-3, DSP-4, DSP-5, DSP-6, DSP-7, DSP-8, DSP-
20 9, DSP-10, DSP-11, DSP-12, DSP-13, DSP-14, DSP-15, DSP-16, DSP-17, DSP-18, CD45, etc. Other methods that do not require the use of a crystalline PTP in order to accomplish oxidation to form the PTP-SN or PTP-SS polypeptide may also be used.

PTPs, whether in isolated or purified form or in whole cells, are subjected to an oxidizing agent such as hydrogen peroxide under conditions and for a time
25 sufficient to permit the formation of the PTP-SN or PTP-SS state. For example, a selected PTP (56 µM) is incubated with 50 µM H₂O₂ for 10 minutes in 50 mM Hepes, pH 7.5, 1 mM EDTA, 200 µM DTT. One µL is digested with trypsin in 50 mM ammonium bicarbonate, pH 8.0, and analyzed using MALDI-TOF mass spectrometry. Ten microliters are boiled for 10 minutes in SDS-loading buffer and analyzed by SDS-PAGE.

To reversibly oxidize the PTP (pulse-chase experiment), 30 μL 'heavy' $\text{H}_2^{18}\text{O}_2$ (2% stock solution, Icon 19 Ox Bow Lane, Summit, NJ, USA) is added to an equal volume of 26 μM PTP1B in degassed buffer (50 mM Hepes, pH 7.5, 1 mM EDTA, 100 μM DTT) giving final concentrations of between 5 and 5×10^4 μM . At 30 minutes, 10 μL of the
5 selected PTP mixture is removed and chased with "light" $\text{H}_2^{16}\text{O}_2$ (>100 fold excess) for two hours and then trypsinized; 20 μL is removed to assay enzyme activity (% inhibition) using pNPP as substrate. The remaining 30 μL of the sample are incubated with DTT (10 mM) and catalase (10 units) for two hours, and the recovered enzyme activity is measured using pNPP as substrate (% recovery). For trypsinolysis, the selected PTP is diluted with
10 50 mM ammonium bicarbonate, pH 8.0, 5 mM DTT, and 0.3 μg of sequencing grade trypsin and incubated at 37 $^\circ\text{C}$ for 12-16 hours. One μL of digest is mixed with saturated α -cyano-4-hydroxycinnamic acid and analyzed with a mass spectrometer.

EXAMPLE 2

15 X-RAY CRYSTALLOGRAPHY ANALYSIS OF PTP1B DOUBLE MUTANT

A PTP1B double mutant was prepared by substituting an alanine residue for the catalytic cysteine residue at position 215 and substituting an alanine residue for the serine residue at position 216 of the wildtype PTP1B using standard site-directed mutagenesis techniques known in the art. The double mutant PTP1B was analyzed by X-
20 ray crystallography using techniques similar to those described in Example 1 for solving the crystal structure of wildtype PTP1B.

Those skilled in the art will recognize, or be able to ascertain, using no more than routine experimentation, many equivalents to the specific embodiments of the
25 invention described herein. Such equivalents are intended to be encompassed by the following claims.

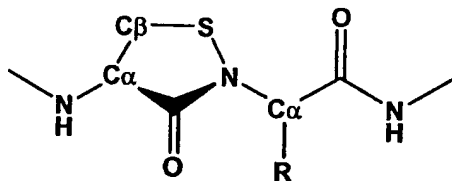
CLAIMS

What is claimed is:

1. An isolated polypeptide comprising the amino acid sequence $-C-(X)_5-R-$ (SEQ ID NO:1), wherein C is cysteine, R is arginine, and X is any amino acid residue, and wherein a sulfur atom of the cysteine is covalently linked to a main-chain nitrogen atom of an adjacent C-terminal amino acid residue.

2. An isolated protein tyrosine phosphatase polypeptide in a cyclic sulfenyl-amide form (PTP-SN).

3. An isolated polypeptide comprising the sequence $-Cys-(X)_5-Arg-$ (SEQ ID NO:1), wherein X is any amino acid residue, and wherein the cysteine residue and the adjacent C-terminal amino acid residue in SEQ ID NO:1 form the following chemical structure



wherein R is the amino acid side chain of the adjacent C-terminal amino acid residue.

4. The polypeptide according to any one of claims 1-3, wherein the polypeptide is selected from the group consisting of PTP1B comprising the amino acid sequence set forth in any one of SEQ ID NOS:24, 26, and 30; cdc14a comprising the amino acid sequence set forth in any one of SEQ ID NOS:85, 87, and 89; cdc14b comprising the amino acid sequence set forth in any one of SEQ ID NOS:91 and 93; cdc25a comprising the amino acid sequence set forth in any one of SEQ ID NOS:67 and 69; cdc25b

comprising the amino acid sequence set forth in any one of SEQ ID NOS:77 and 79; cdc25c comprising the amino acid sequence set forth in any one of SEQ ID NOS:81 and 83; DSP-3/JSP-1 comprising the amino acid sequence set forth in SEQ ID NO:97; and DEP-1 comprising the amino acid sequence set forth in any one of SEQ ID NOS:38 and 40.

5. The polypeptide according to any one of claims 1-3, wherein the polypeptide is PTP1B comprising the amino acid sequence set forth in any one of SEQ ID NOS:24, 26, and 30.

6. An isolated protein tyrosine phosphatase (PTP) enzyme comprising a sequence [I/V]HCXAGXXR[S/T]G (SEQ ID NO:106), wherein X is any amino acid, and wherein cysteine in SEQ ID NO:106 and the adjacent C-terminal residue together form a cyclic sulfenyl-amide group between the sulfur atom of the cysteine and the main-chain nitrogen atom of the adjacent C-terminal residue.

7. The PTP according to claim 6, wherein the PTP is selected from the group consisting of (a) PTP1B comprising the amino acid sequence set forth in any one of SEQ ID NOS:24, 26, and 30 and (b) DEP-1 comprising the amino acid sequence set forth in any one of SEQ ID NOS:38 and 40.

8. The PTP according to claim 6 wherein the PTP is PTP1B comprising the amino acid sequence set forth in any one of SEQ ID NOS:24, 26, and 30.

9. A method of making a protein tyrosine phosphatase in a cyclic sulfenyl-amide form (PTP-SN) comprising subjecting a biological sample comprising a PTP that comprises the sequence C-(X)₅-R (SEQ ID NO:1), wherein X is any amino acid, to oxidation conditions for a time and under conditions sufficient to induce the cysteine residue of SEQ ID NO:1 to form a cyclic sulfenyl-amide with the adjacent C-terminal residue.

10. A method for identifying a compound that hinders reduction of a cyclic sulfenyl-amide protein tyrosine phosphatase (PTP-SN) comprising:

- (a) introducing a PTP-SN to a test compound to form a composition;
- (b) adding a reducing agent to the composition of (a) under conditions and for a time sufficient to permit binding of the test compound to the PTP-SN; and
- (c) analyzing the composition to determine the presence or absence of PTP-SN.

11. The method of claim 10, wherein the reducing agent is selected from the group consisting of beta-mercaptoethanol, dithiothreitol (DTT), dithioerythritol (DTE), glutathione, and a phosphine.

12. The method according to claim 10, wherein the step of analyzing comprises performing a functional assay on the composition to determine PTP catalytic activity.

13. A method for identifying a compound that binds to a protein tyrosine phosphatase sulfenyl-amide form (PTP-SN) comprising:

- (a) contacting a PTP-SN with a test compound; and
- (b) determining binding of the compound to the PTP-SN, thereby identifying a compound that binds to the PTP-SN.

14. The method of claim 13 wherein the compound does not bind to a PTP-SN that has been converted to a catalytically active PTP by reducing conditions.

15. The method of claim 13 wherein the step of determining binding comprises performing X-ray crystallographic analysis.

16. The method of either claim 10 or claim 13 wherein the compound stabilizes the PTP-SN in the oxidized state.

17. The method according to either claim 10 or claim 13, wherein the PTP is PTP1B comprising the amino acid sequence set forth in any one of SEQ ID NOS:24, 26, and 30.

18. The method according to either claim 10 or claim 13, wherein the PTP is selected from the group consisting of PTP1B comprising the amino acid sequence set forth in any one of SEQ ID NOS:24, 26, and 30; cdc14a comprising the amino acid sequence set forth in any one of SEQ ID NOS:85, 87, and 89; cdc14b comprising the amino acid sequence set forth in any one of SEQ ID NOS:91 and 93; cdc25a comprising the amino acid sequence set forth in any one of SEQ ID NOS:67 and 69; cdc25b comprising the amino acid sequence set forth in any one of SEQ ID NOS:77 and 79; cdc25c comprising the amino acid sequence set forth in any one of SEQ ID NOS:81 and 83; DSP-3/JSP-1 comprising the amino acid sequence set forth in SEQ ID NO:97; and DEP-1 comprising the amino acid sequence set forth in any one of SEQ ID NOS:38 and 40.

19. A method for identifying a compound that modulates or hinders reduction of a cyclic sulfenyl-amide protein tyrosine phosphatase-1B (PTP1B-SN) comprising:

- (a) obtaining crystalline PTP1B-SN;
- (b) introducing a test compound to the crystalline PTP1B-SN under conditions and for a time sufficient to permit binding of the test compound to the PTP1B-SN; and
- (c) analyzing the crystalline PTP1B-SN to determine whether the test compound binds thereto.

20. A method for identifying a compound that hinders reduction of a cyclic sulphenyl-amide protein tyrosine phosphatase-1B (PTP1B-SN) comprising:

- (a) introducing a test compound to the PTP1B-SN to form a composition;
- (b) adding a reducing agent to the composition of (a), under conditions and for a time sufficient to permit binding of the test compound to the PTP1B-SN; and
- (c) analyzing the composition to determine the presence or absence of PTP1B-SN.

21. A double mutant protein tyrosine phosphatase (PTP) polypeptide having the amino acid sequence $-CS(X)_4-R-$ set forth in SEQ ID NO:109, wherein X is any amino acid, said mutant PTP comprising a substitution of the cysteine in SEQ ID NO:1 and a substitution of the amino acid that is the adjacent C-terminal residue to the cysteine residue.

22. The double mutant PTP of claim 21 wherein the catalytic domain of the double mutant PTP possesses a three-dimensional structure that is substantially similar to the three-dimensional structure of the catalytic domain of the corresponding PTP-SN.

23. A double mutant protein tyrosine phosphatase (PTP) polypeptide having the amino acid sequence $-H-C-S-X-G-X-G-R-X-G-$ set forth in SEQ ID NO:21, wherein X is any amino acid, said mutant PTP comprising (a) a substitution of the cysteine in SEQ ID NO:21, and (b) a substitution of the serine that is adjacent to the cysteine residue.

24. The double mutant PTP of claim 23 wherein the catalytic domain of the double mutant PTP possesses a three-dimensional structure that is substantially similar to the three-dimensional structure of the catalytic domain of the corresponding PTP-SN.

25. The double mutant PTP polypeptide according to either claim 21 or claim 23, wherein the PTP is selected from the group consisting of PTP1B comprising the amino acid sequence set forth in any one of SEQ ID NOS:24, 26, and 30 and DEP-1 comprising the amino acid sequence set forth in any one of SEQ ID NO:38 and 40.

26. The double mutant PTP according to claim 21 wherein the cysteine residue is substituted with an alanine residue.

27. The double mutant PTP according to claim 21 wherein the adjacent C-terminal residue is substituted with an alanine residue.

28. The double mutant PTP according to claim 21 wherein the cysteine residue is substituted with an alanine residue and wherein the adjacent C-terminal residue is a serine residue that is substituted with an alanine residue.

29. A double mutant protein tyrosine phosphatase-1B (PTP1B) polypeptide comprising the amino acid sequence of SEQ ID NO:109 in which the cysteine in SEQ ID NO:109 is substituted and the serine in SEQ ID NO:109 is substituted, wherein the cysteine is located at position number 215 in any one of SEQ ID NOS:24, 26, and 30 and the serine is located at position number 216 in any one of SEQ ID NOS:24, 26, and 30, and wherein the double mutant PTP1B is at least 80% identical to the amino acid sequence set forth in in any one of SEQ ID NOS:24, 26, and 30.

30. The double mutant of claim 29 wherein the double mutant PTP1B is at least 90% identical to the amino acid sequence set forth in in any one of SEQ ID NOS:24, 26, and 30.

31. The double mutant of claim 29 wherein the double mutant PTP1B is at least 95% identical to the amino acid sequence set forth in in any one of SEQ ID NOS:24, 26, and 30.

32. The double mutant of claim 29 wherein the double mutant PTP1B is at least 99% identical to the amino acid sequence set forth in in any one of SEQ ID NOS:24, 26, and 30.

33. The double mutant PTP according to claim 29, wherein cysteine located at position 215 is substituted with a alanine residue, and wherein serine located at position 216 is substituted with an alanine residue.

34. The double mutant PTP according to claim 29 comprising the amino acid sequence set forth in SEQ ID NO:110.

35. An antibody, or an antigen-binding fragment thereof, that binds to at least one polypeptide selected from the group consisting of

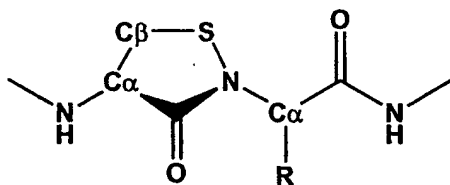
(a) double mutant protein tyrosine phosphatase (PTP) polypeptide having the amino acid sequence $-CS(X)_4-R-$ set forth in SEQ ID NO:109, wherein X is any amino acid, said mutant PTP comprising a substitution of the cysteine in SEQ ID NO:1 and a substitution of an amino acid that is an adjacent C-terminal residue to the cysteine residue; wherein the catalytic domain of the double mutant PTP possesses a three-dimensional structure that is substantially similar to the three-dimensional structure of the catalytic domain of the corresponding PTP-SN;

(b) double mutant protein tyrosine phosphatase (PTP) polypeptide having the amino acid sequence $-H-C-S-X-G-X-G-R-X-G-$ set forth in SEQ ID NO:21, wherein X is any amino acid, said mutant PTP comprising (a) a substitution of the cysteine in SEQ ID NO:21, and (b) a substitution of serine that is adjacent to the cysteine residue; wherein the catalytic domain of the double mutant PTP possesses a three-dimensional

structure that is substantially similar to the three-dimensional structure of the catalytic domain of the corresponding PTP-SN;

(c) a PTP-SN polypeptide comprising comprising the amino acid sequence $-C(X)_5-R-$ (SEQ ID NO:1), wherein C is cysteine, R is arginine, and X is any amino acid residue, and wherein a sulfur atom of the cysteine is covalently linked to a main-chain nitrogen atom of an adjacent C-terminal amino acid residue; and

(d) a PTP-SN polypeptide comprising the sequence Cys-(X)₅-Arg (SEQ ID NO:1), wherein X is any amino acid residue, and wherein the cysteine residue and an adjacent C-terminal amino acid residue in SEQ ID NO:1 form the following chemical structure



wherein R is the amino acid side chain of the adjacent C-terminal amino acid residue.

36. The antibody of claim 35 wherein the antibody or antigen binding fragment thereof binds to at least two polypeptides.

37. The antibody of claim 35 wherein the antibody or antigen binding fragment thereof binds to at least one double mutant PTP polypeptide and to at least one PTP-SN polypeptide.

38. The antibody according to claim 35 wherein the antibody is a polyclonal antibody or a monoclonal antibody.

39. The antibody according to claim 35 wherein the antigen-binding fragment is selected from the group consisting of a Fab, a Fab', a F(ab')₂, a Fv, and a Fd fragment.

40. The antibody according to claim 35 wherein the antibody is selected from the group consisting of a chimeric antibody, a humanized antibody, and a single chain antibody.

41. The antibody according to claim 38 wherein the monoclonal antibody is selected from the group consisting of a mouse monoclonal antibody, a human monoclonal antibody, a rat monoclonal antibody, and a hamster monoclonal antibody.

42. A hybridoma cell that produces the monoclonal antibody according to claim 38.

43. A host cell that expresses the antibody according to any one of claims 35-41.

44. A composition comprising an antibody, or antigen-binding fragment thereof, according to any one of claims 35-41 and a physiologically acceptable carrier.

45. A method for identifying an agent that binds specifically to a double mutant protein tyrosine phosphatase (PTP) polypeptide comprising (a) contacting a double mutant PTP according to either claim 21 or claim 23 with a candidate agent under conditions and for a time sufficient to permit interaction between the mutant PTP and the candidate agent; (b) contacting the corresponding wildtype PTP polypeptide with the candidate agent under conditions and for a time sufficient to permit interaction between the wildtype PTP and the candidate agent; (c) comparing the level of binding of the candidate agent to the mutant PTP with the level of binding of the candidate agent to the wildtype

PTP, wherein an increased level of binding to the mutant PTP relative to the level of binding to the wildtype PTP indicates that the agent specifically binds to the mutant PTP polypeptide.

46. A method for identifying an agent that alters reduction of a protein tyrosine phosphatase sulfenyl-amide form (PTP-SN) comprising: (a) contacting a double mutant PTP polypeptide according to either claim 21 or claim 23 with a candidate agent under conditions and for a time sufficient to permit interaction between the mutant PTP and the candidate agent; (b) contacting the corresponding wildtype PTP polypeptide with the candidate agent under conditions and for a time sufficient to permit interaction between the wildtype PTP and the candidate agent; (c) determining a level of binding of the candidate agent to the mutant PTP; (d) determining a level of binding of the candidate agent to the wildtype PTP; and (e) comparing the level of binding of the candidate agent to the mutant PTP relative to the level of binding of the candidate agent to the wildtype PTP, wherein an increased or decreased level of binding of the candidate agent to the mutant PTP indicates that the agent alters reduction of a PTP-SN.

1/16

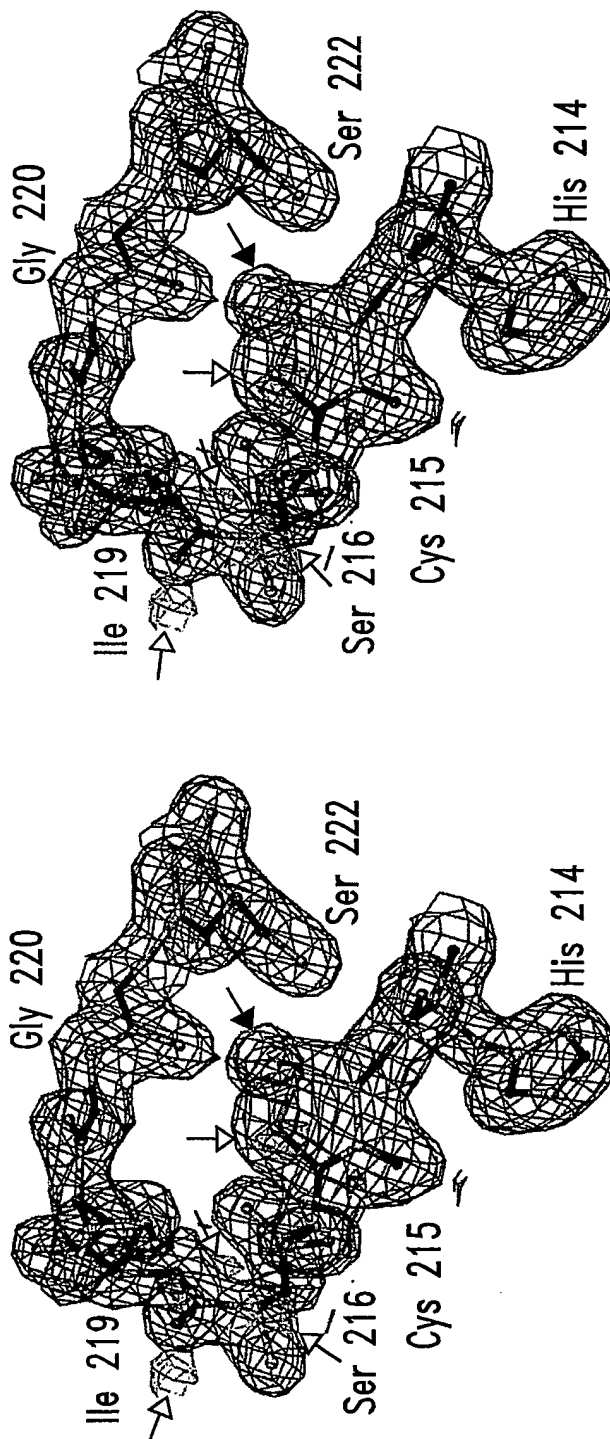


FIG. 1A

BEST AVAILABLE COPY

2/16

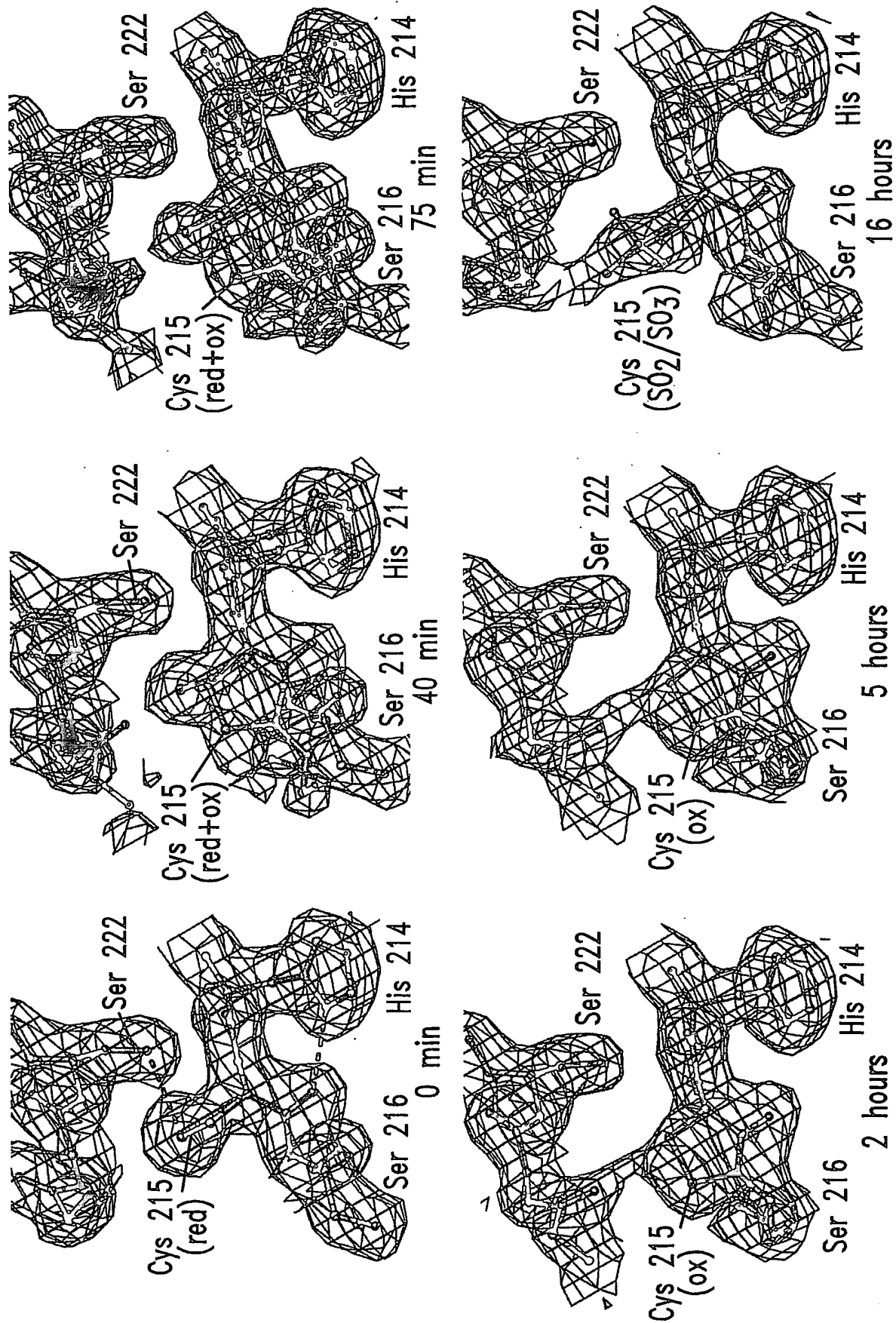


FIG. 1B

3/16

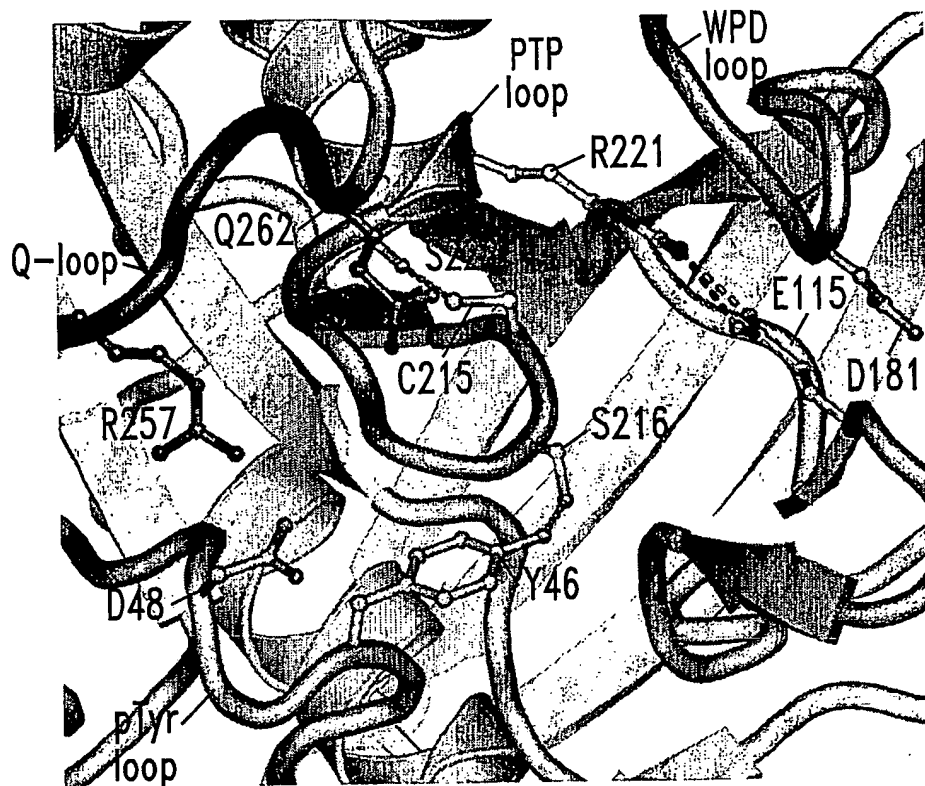


FIG. 2A

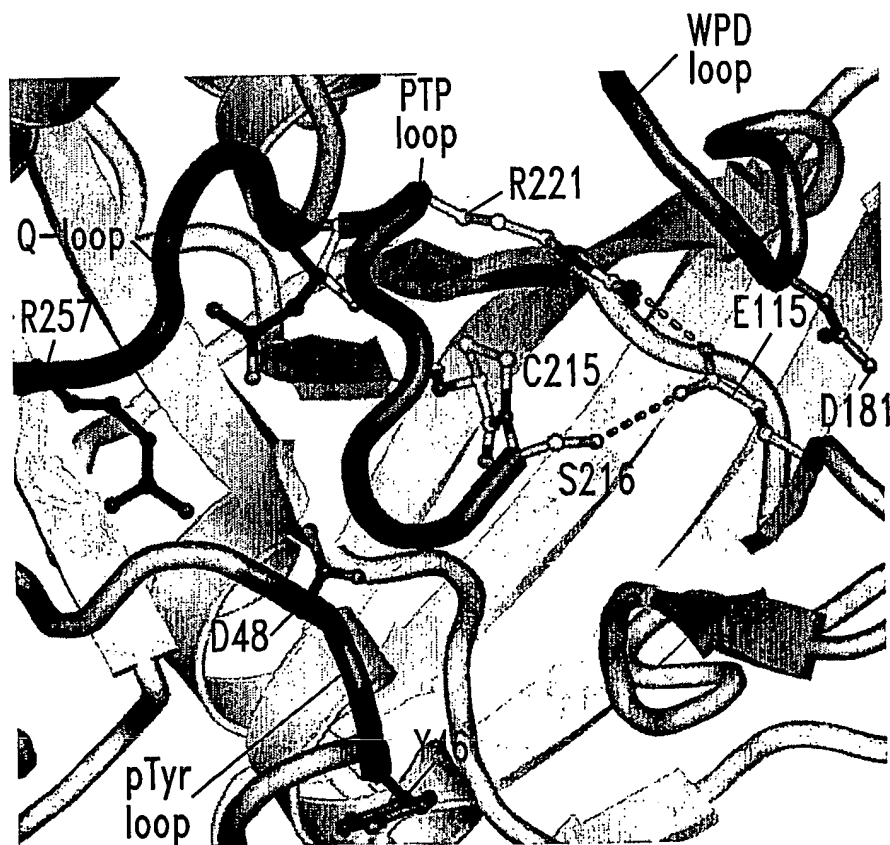
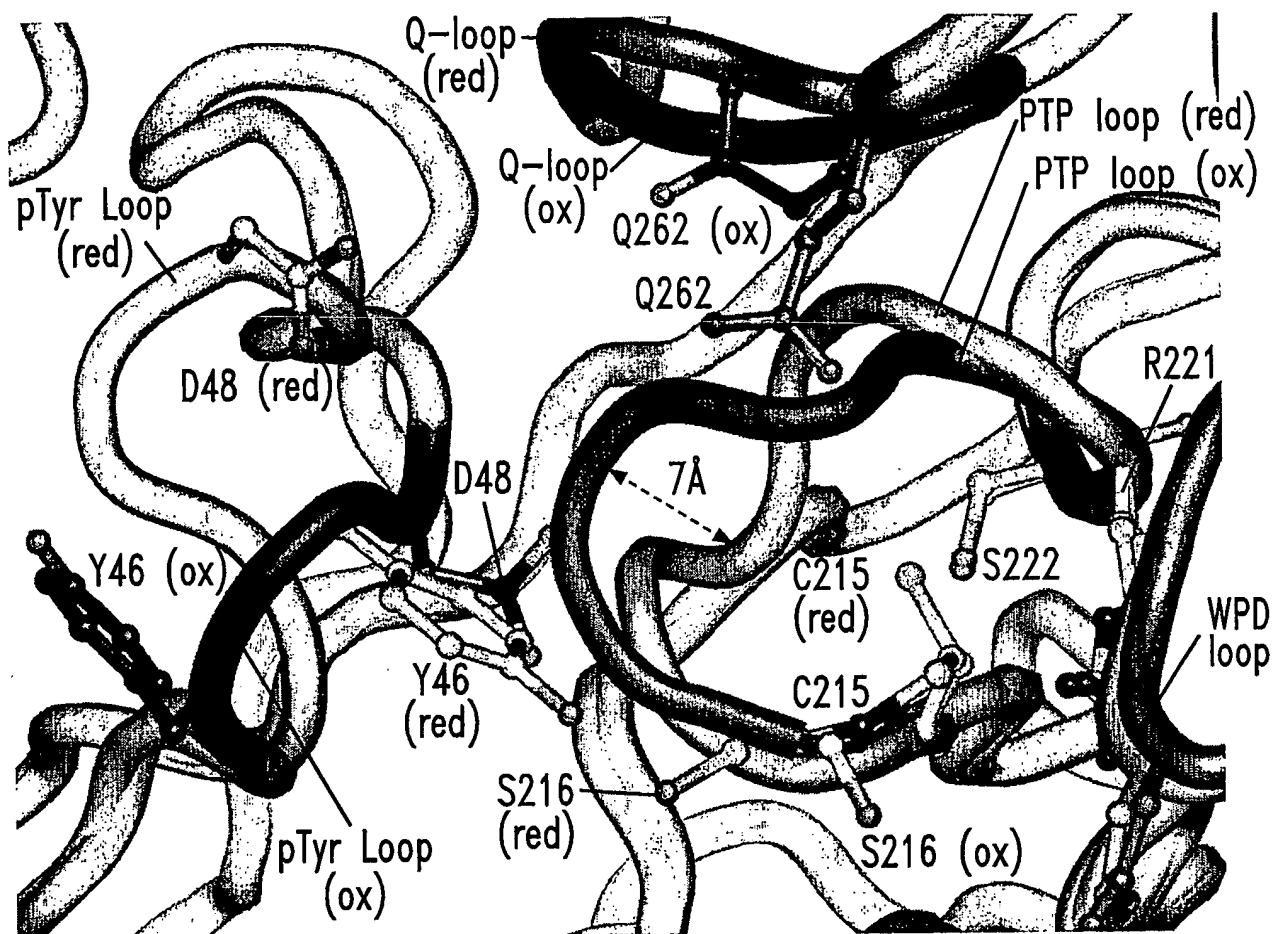


FIG. 2B

BEST AVAILABLE COPY

4/16

*FIG. 2C*

BEST AVAILABLE COPY

5/16

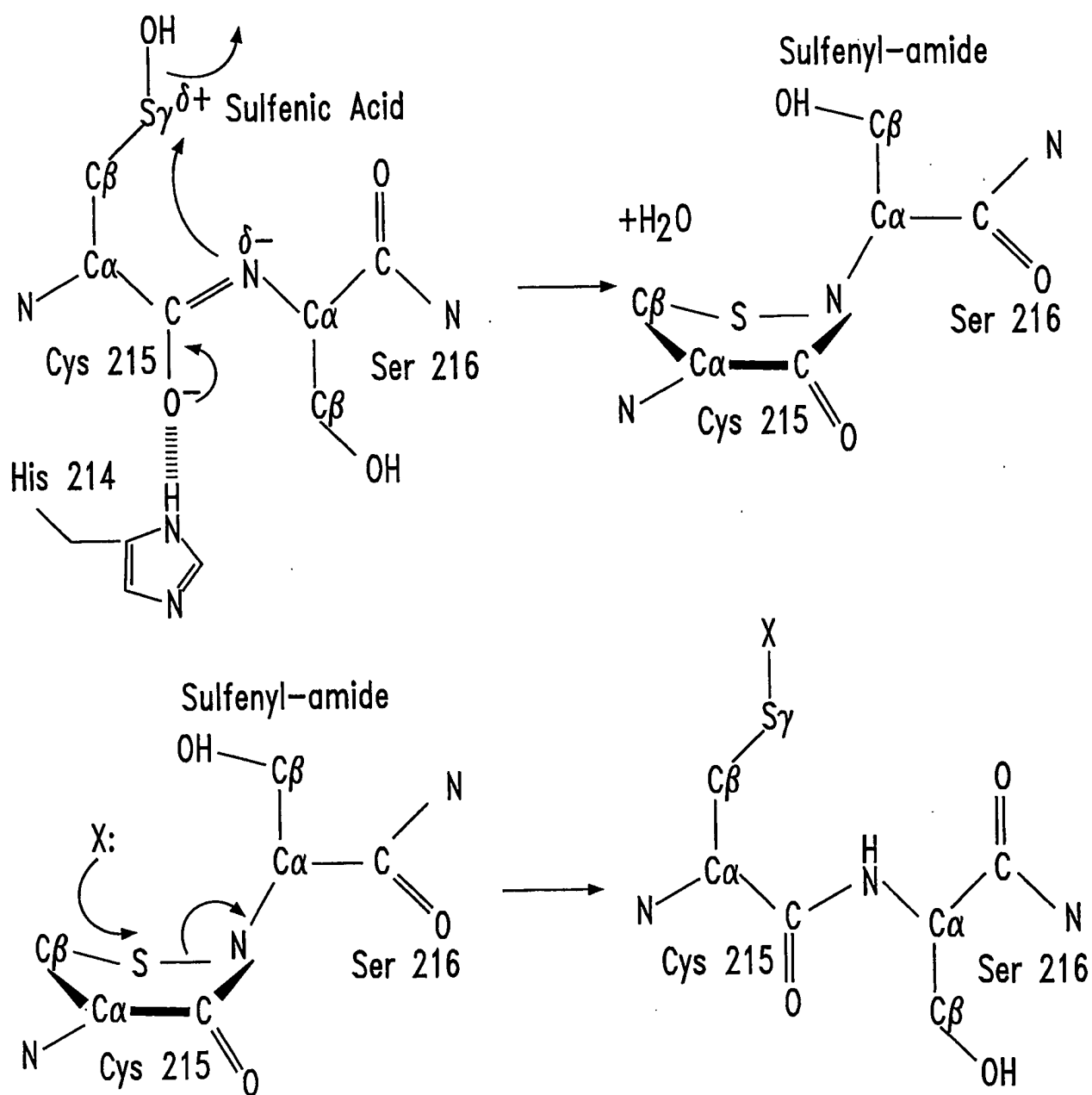


FIG. 2D

6/16

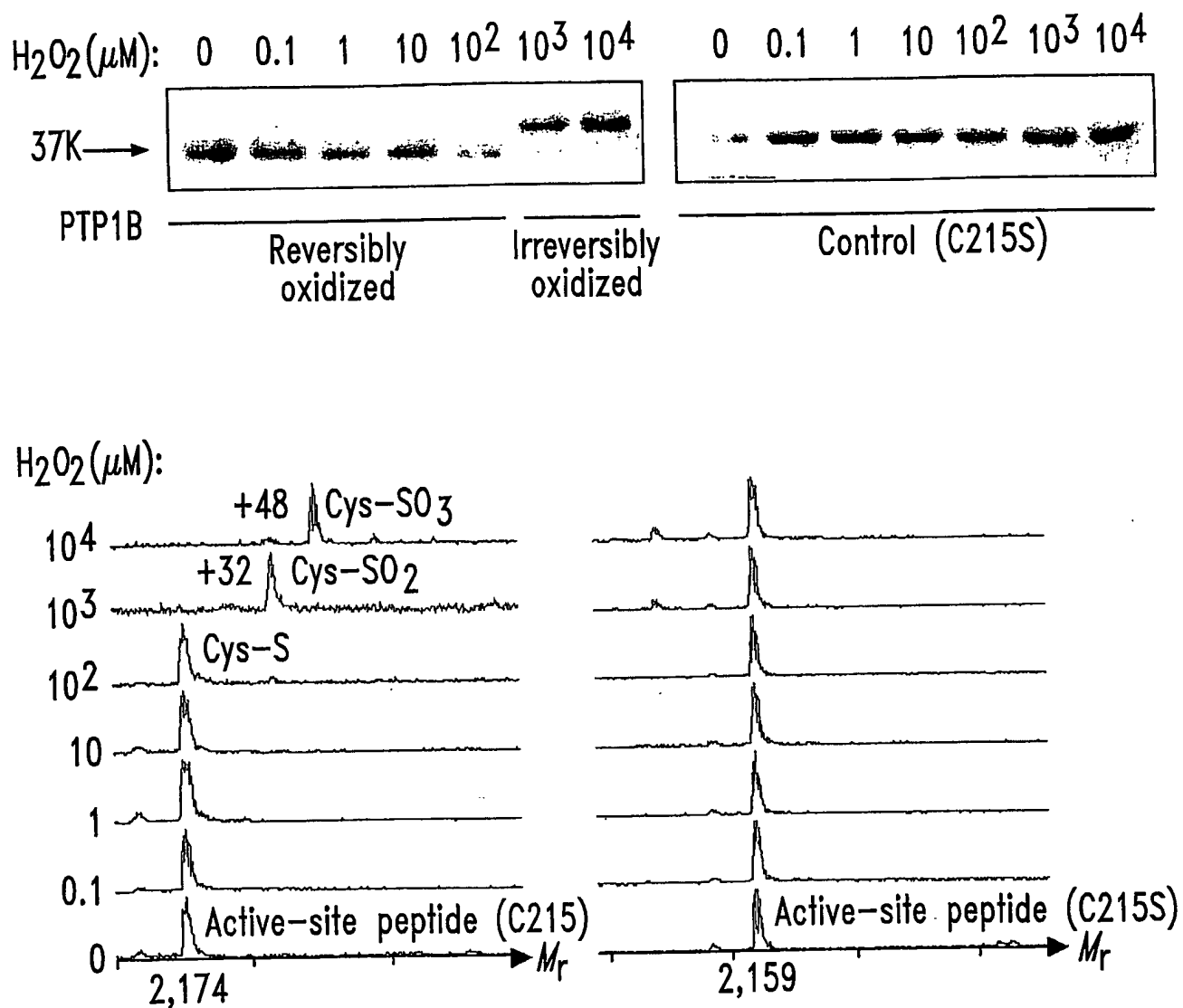


FIG. 3A

7/16

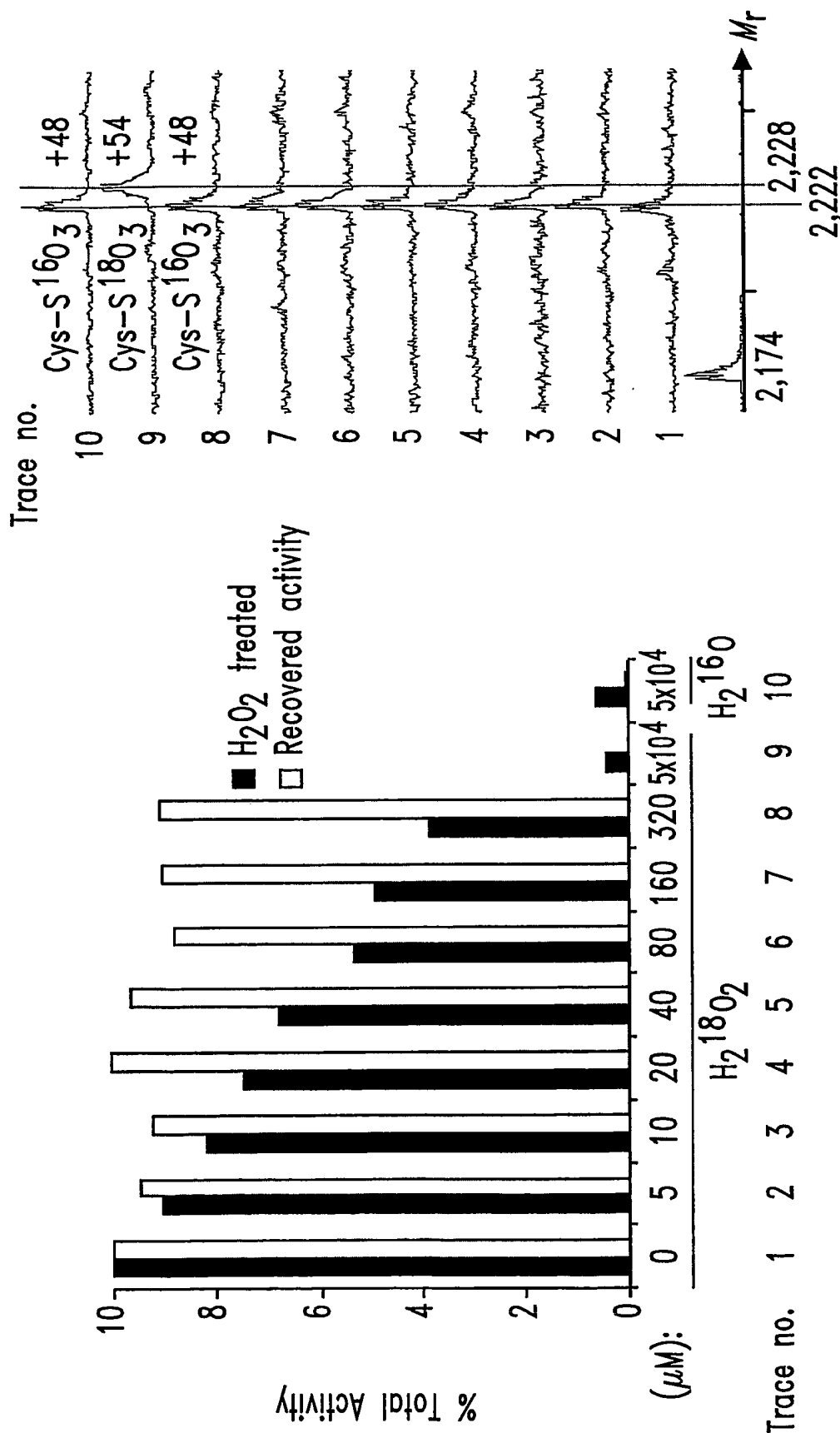


FIG. 3B

8/16

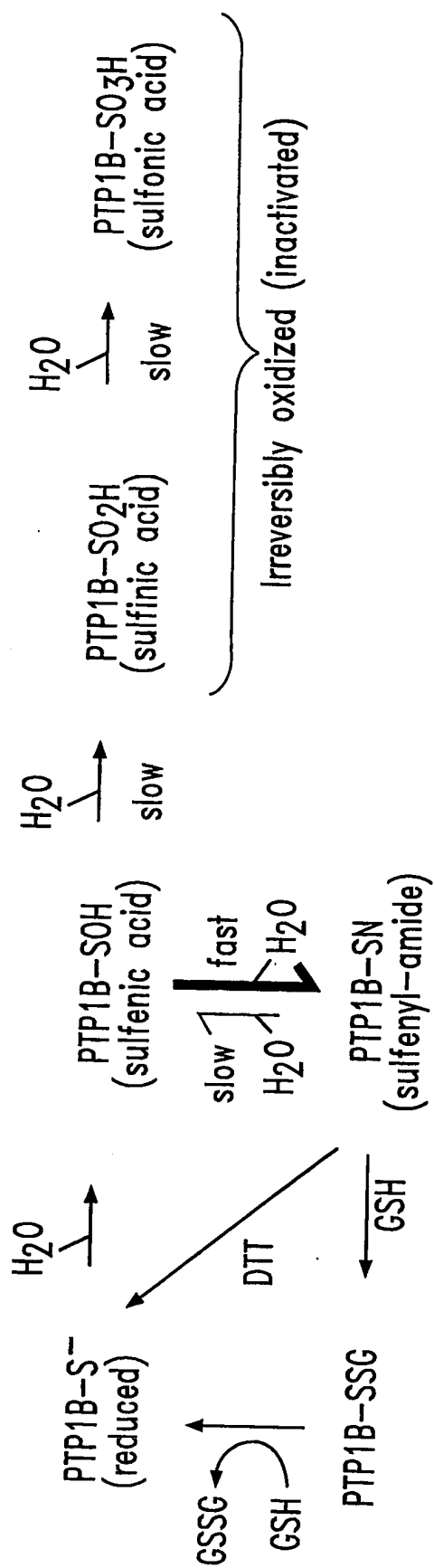


FIG. 4A

9/16

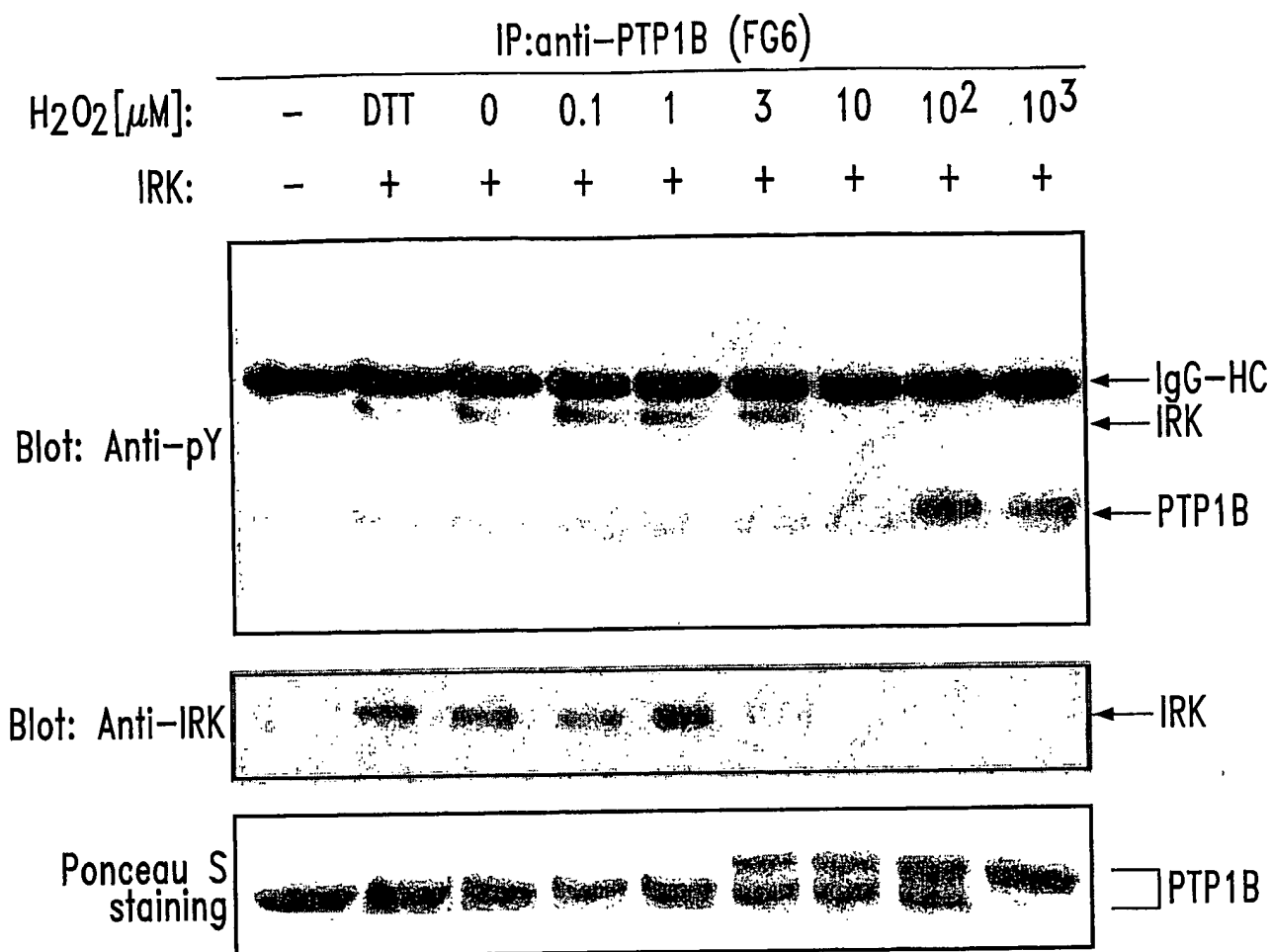


FIG. 4B

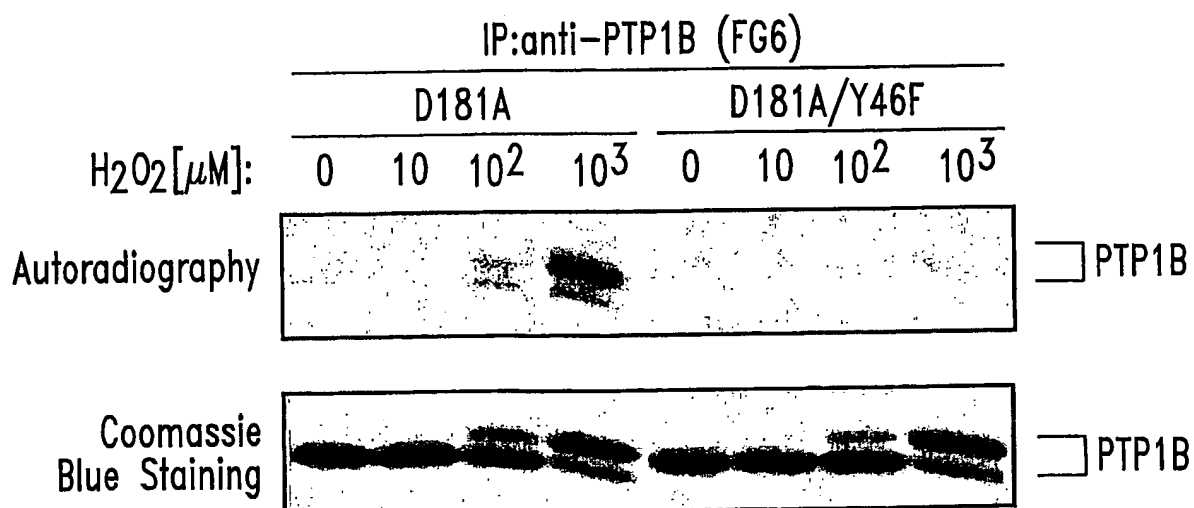
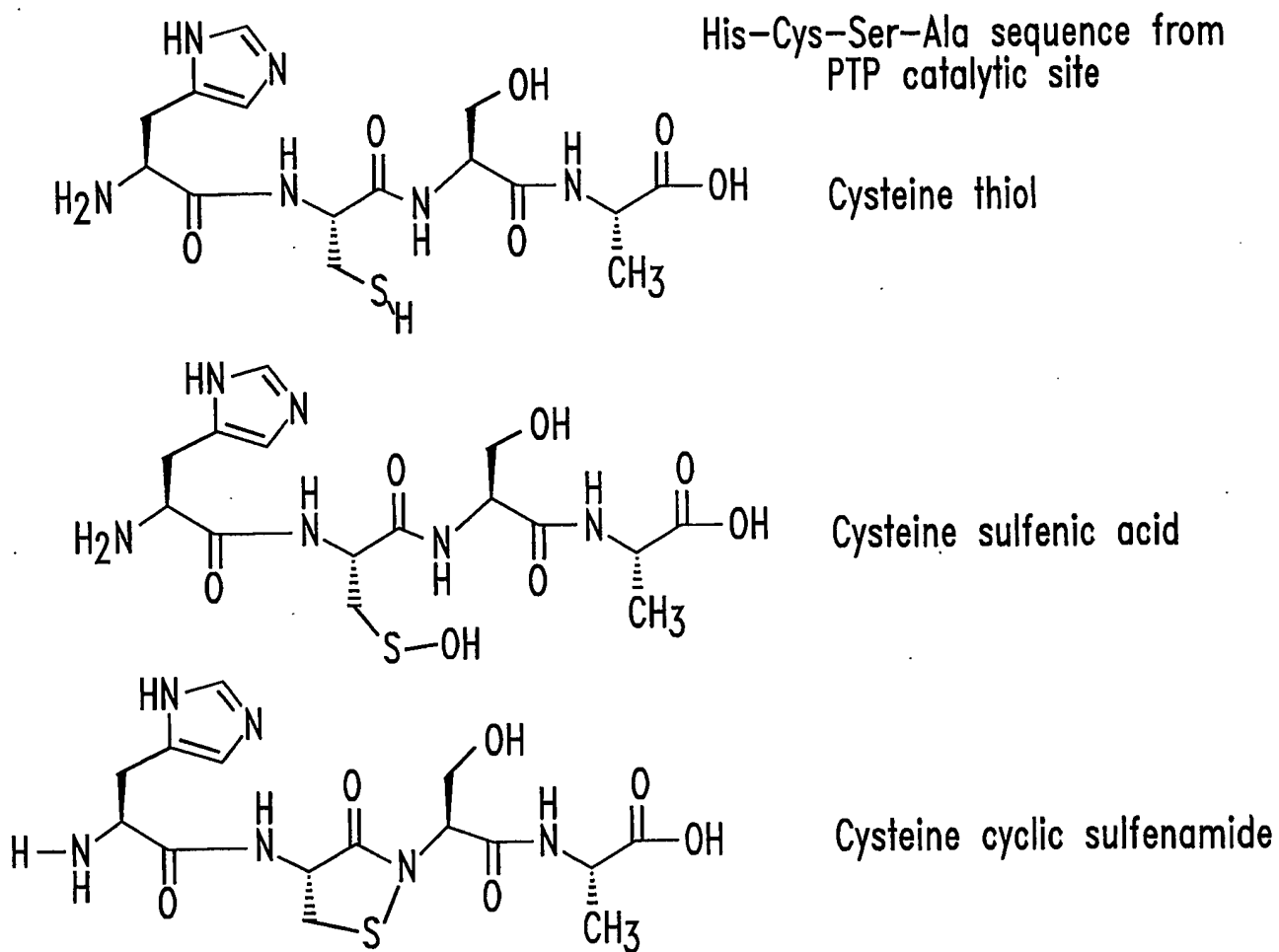


FIG. 4C

10/16

*FIG. 5*

11/16

MPEP
 PEST
 BDP1
 PTP-1C
 SH-PTP2
 PTP-nu
 PTP-kappa
 PTP-rho
 PTP-delta
 PTP-sigma
 LAR
 HeTP
 PTP-epsilon
 PTP-gamma
 PTP-zeta
 CD45
 PTP-beta
 PTP-eta
 GLEPP1
 PTP-GWC1:
 PTP-de1ta2
 PTP-sigma2
 LAR2
 HeTP2
 PTP-epsilon2
 TC
 PTP-1B
 MEG
 IA2
 IA-2beta
 CD45-2
 HPC-PTP1
 STEP
 PEZ
 PTP-D1
 MEG1
 PTP-H1
 PTP-L1

201 210 220 230 240 250 260 270 280 290 300
 FNNETRIIYQFHYKNWPDHVP - SSIDPILQIWMRCYQED - DC - VPICHCAGCGRTGIVCAVDYTWMLLKDGIPKNE
 FQNESRLYQFHYVNWPDHVP - SSFDSILDMISLMKYQEH - ED - VPICHCAGCGRTGAICAIDYTWMLLKAGKIPKEF
 FQKESRSVQLQYMSWPDHVP - SSPDHMLAWEEARRLOGS - GP - EPLVHCAGCGRTGLCTVDYVRQLLTQMIPPDF
 DNGDLIREIWHYQYLSWPDHVP - SEPGVLSFLDQINQRQESLPHA - GPIVHCAGIGRTGIIIVIDMLMENISTKGLDCDI
 GQGNTERTVQYHFTWPDHVP - SDPGVLDLFLVHHKQESIMDA - GPVHCAGIGRTGTFIVIDILIDIIREKGVDCDI
 VH-EIRE - IROFHTGPDHVP - YHATGLGFVRQK - SKSPPSA - GPLVHCAGAGRTGCFIVIDIMDMAEREGV - V
 YN-EIRE - VKQFHTGPDHVP - YHATGLSFIRRVK - LSNPPSA - GPIVHCAGAGRTGCTIVIDIMDMAEREGV - V
 YH-EIRE - LRLFHTSWPDHVP - CYATGLGFVRQK - FLNPPEA - GPIVHCAGAGRTGCFIADITMLDMAENEGV - V
 SS-EKRE - VROFQTAWPDHVP - EHPTPFLAFRRVK - TCNPPDA - GPMVHCAGVGRGTGCFIVIDAMLERIKHEKT - V
 SS-EKRE - VROFQTAWPDHVP - EYPTPFLAFRRVK - TCNPPDA - GPMVHCAGVGRGTGCFIVIDAMLERIKHEKT - V
 SS-EKRE - LROFQMAWPDHVP - EYPTPILAFRRVK - ACNPLDA - GPMVHCAGVGRGTGCFIVIDAMLERMKHEKT - V
 DM-TNRKQRLITQFHTSWPDHVP - FTPIGMLKFLKKVK - ACNPQYA - GAIVHCAGVGRGTGTFIVIDAMLMHTERK - V
 PD-GCKAP - RLVSQHLFTSWPDHVP - FTPIGMLKFLKKVK - TLNPVHA - GPIVHCAGVGRGTGTFIVIDAMMMHAEQK - V
 QKGNPKGRQNERVVIQYHTQWPDHVP - EYALPVLTFVRRSS - AARMPET - GPMVHCAGVGRGTGTFIVIDSMLOQIKDKST - V
 SQ-KGRPSGRVVTQYHTQWPDHVP - EYSLPVLTFVRKAA - YAKRHAV - GPMVHCAGVGRGTGTYIVLDSMLQIQHEGT - V
 -KEKATGREVTHIQFTSWPDHVP - EDPHLLKLRVRN - AFSNFFS - GPIVHCAGVGRGTGTYIGIDAMLEGAENK - V
 EQLDAHLIRHFHYTVWPDHVP - ETTQSLIQFVRTVDYINRSPGA - GPTVHCAGVGRGTGTFIALDRILQQLDSKDS - V
 QTSSEHPL - RQFHTSWPDHVP - DTDLLINFRYLVRDYMKSQPE - SPILVHCAGVGRGTGTFIADRLIYOIENENT - V
 DEMQD - VMHFNVTAWPDHVP - TAAAESILQFVHMVRQQAATKS - K - GPMIHCAGVGRGTGTFIALDRLLQHIRDHEF - V
 GDCMTVR - QFTGWPEHVP - ENTPLIHFVKLR - TSRAHDT - TPMVHCAGVGRGTGVFIALDHLTQHINNHD - V
 -R - DGQSRTRVQFQTDWPEQVGP - KSGEGFIDFQGVHKTKEQFGOD - GPIVHCAGVGRGTGVFITLSIVLERMYEGV - V
 -R - DGQSRTRVQFQTDWPEQVGP - KSGEGFIDFQGVHKTKEQFGOD - GPIVHCAGVGRGTGVFITLSIVLERMYEGV - V
 -R - DGQSRTRVQFQTDWPEQVGP - KSGEGFIDFQGVHKTKEQFGOD - GPIVHCAGVGRGTGVFITLSIVLERMYEGV - V
 -R - ENKSRQIRQFHFHGWPEVGP - SDGKGMISIIAAVQKQQQSGNH - PITVHCAGAGRTGTFICALSTVLERVKAEGI - L
 -QPQARQEEQVRVVRQFHFHGWPEVGP - AEGKGMIDIIAAVQKQQQSGNH - PITVHCAGAGRTGTFICALSTVLERVKAEGI - L
 -TTQETREILHFHYTTWPDHVP - ESPASFLNLFKVRSGSLNPDH - GPAVHCAGIGRSGTFSIVDTCLVLMKGGD - I
 -NSGETRTISHFHYTTWPDHVP - ESPASFLNLFKVRSGSLNPDH - GPAVHCAGIGRSGTFSIVDTCLVLMKGGD - I
 -EERQKRQVTHFQFVSWPDHVP - SSAASLIDFLRVRNQSLAVSNMGARSKGQCEPPIVHCAGIGRTGTFICALSTVLERVKAEGI - L
 -QTQETRTLTFHFVSWPAEGTP - ASTRPLLDFFRRKVKCYGRSC - PIIVHCSDGAGRTGTYILIDMVLNRMKAGVK - EI
 -QTNETRTVTFHFVSWYDRGVP - SSSRSLDFRRKVKCYGRSC - PIIVHCSDGAGRTGTYILIDMVLNRMKAGVK - EI
 -KRKDSRTVYQYTNWVSEQLP - AEPKELISMIVQVVKQLPKQNSSEGNKHH - KSTPLLIHCRDSQQTGIFCALLNLESAETEVEV - V
 -QGSHTQHKVHYVTSWPDHKT - DSAQPLQLMLDVEEDRLASQGR - GPVHCAGIGRTGCFIATISICQQLKEEGV - V
 -SGTEERGLKHYVTSWPDQKTP - DRAPPLHLVREVEEAAQEGPH - CAPIVHCAGIGRTGCFIATISICQQLRQEGV - V
 -LSGQERTVWHLQYTDWPDHGPC - EDVQGLSYLEEIQSVRRHTNSMLEGTN - RHPPIVHCAGVGRGTGVLILSELMICYLEHNEK - V
 -LTGQERTVWHLQYTDWPDHGPC - EDLKGFLSYLEEIQSVRRHTNSTSD - PQS - PNPPLLVHCAGVGRGTGVLILSELMICYLEHNEK - V
 -EKNESRPLTQIYIAWPDHVP - DDSSDFLFVCHVRNKR - AG - KEEPPVHCAGIGRTGVLITMETAMCLIECNOQ - V
 -QTGEEHTVTHLQVVAWPDHVP - DDSSDFLFVCHVRNKR - AG - KEEPPVHCAGIGRTGVLITMETAMCLIECNOQ - V
 -QREVHRHISHLNFTAWPDHDT - SQPDDLLTFISYMRHIIH - RSGPIIHCAGIGRSGTLICIDVWGLISQDL - F
 CXXXXX

FIG. 6

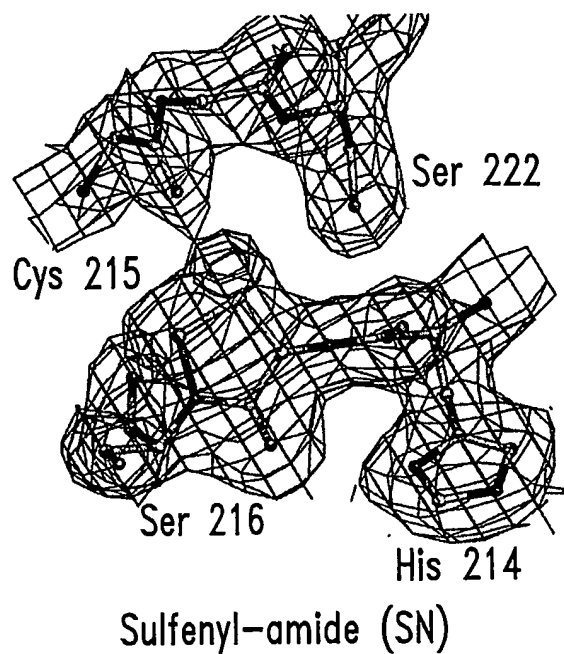
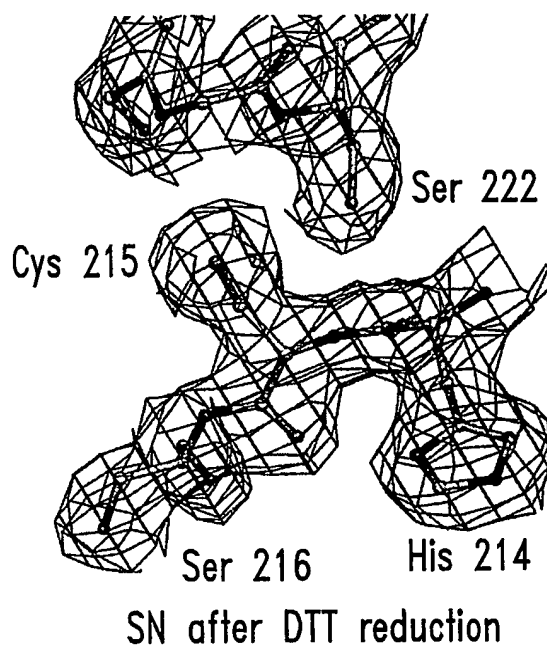
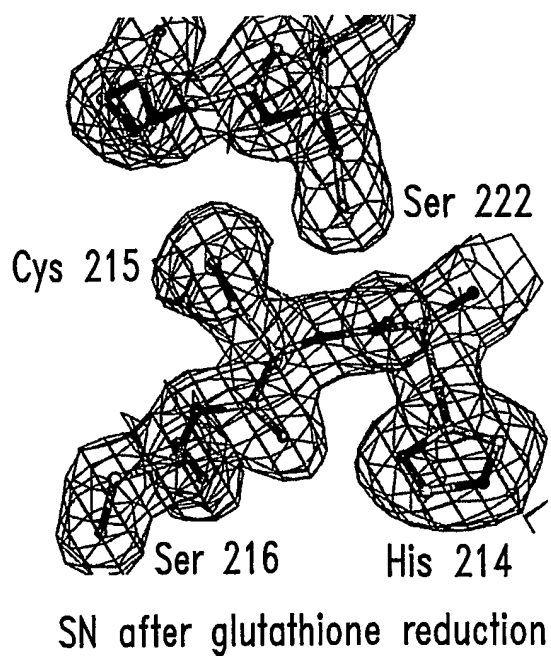
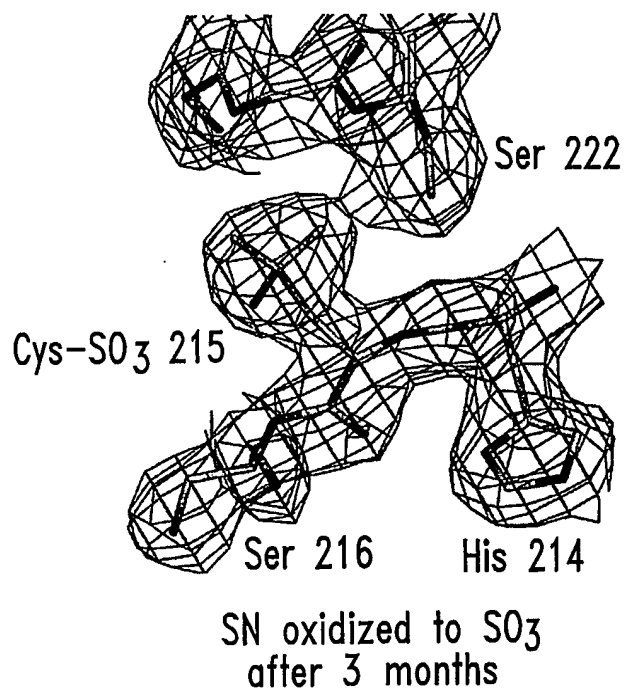
12/16

MKP-1
 MKP-2, 4
 PYST1
 MKP-4
 MKP-5
 MKP-7
 PYST-2
 PAC1
 hVH-5
 EPM2
 VHR
 STYXb
 STYX-2
 STYX-3
 WO01/64911
 MKP- Consensus 1:
 PTEN
 TPTE
 TPIP-alpha
 XM 085008
 ALI37707
 KAP
 MTM1 (PIP3 substrate)
 MTMR3
 PRL-1
 Hprl3
 PIR1
 HsGAK
 ACP-1
 CDC14B
 CDC25B
 AC004099 - DSP- 1
 AA915932 - DSP- 2
 AA374753 - DSP- 3
 AI031656 - DSP- 4
 AA314946 - DSP- 5
 AI208559 - DSP- 6
 AA602372 - DSP- 7
 AI025489 - DSP- 8
 AI372800 - DSP- 9
 N70334 - DSP-10
 AA479435 - DSP-11
 AC008081 - DSP-12
 AC010189 - DSP-13
 AC018511 - DSP-14
 AK001790 - DSP-15
 AC007619 - DSP-16
 AL392111 - DSP-17
 BF377364 - PTP-SN
 CONSENSUS MOTIF

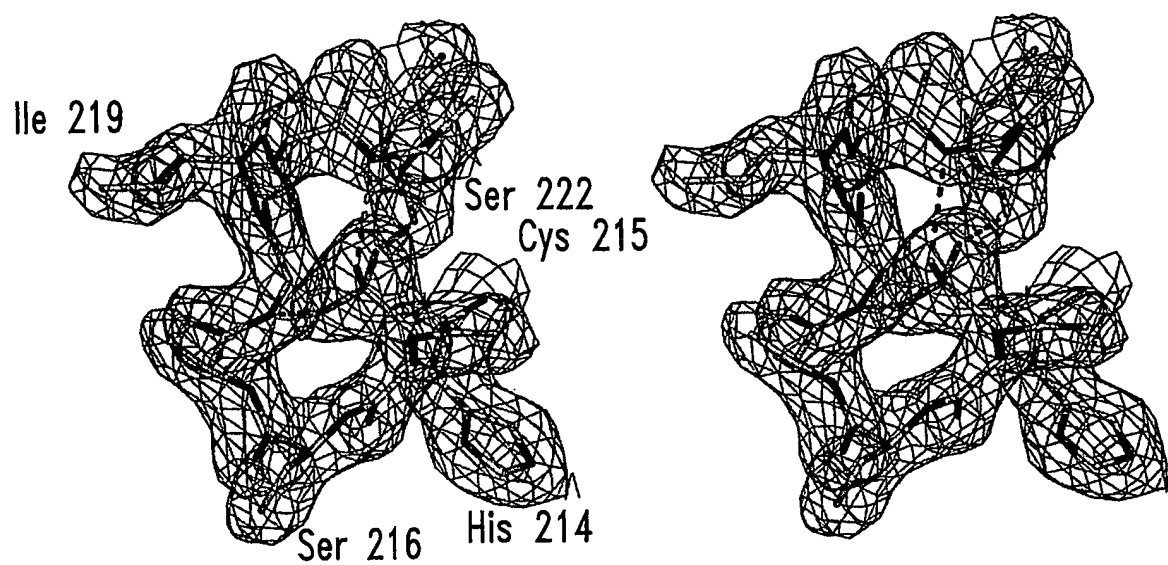
GGRV FVHCQAGISRSATIC-LAYLM
 RGRV LVHCQAGISRSATIC-LAYLM
 NCGV LVHCLAGISRSVTVT-VAYLM
 NCGV LVHCLAGVSRSVTVT-VAYLM
 GGV LVHCEAGISRSPTIC-MAYLM
 NGCV LVHCLAGISRSATIA-IAYIM
 KCGV LVHCLAGISRSVTVT-VAYLM
 GGRV LVHCQAGISRSATIC-LAYLI
 SCQV IVHCLAGISRSATIA-IAYIM
 GHIV VVHCNAGVGRSTAAV-CGWLQ
 NGRV LVHCREGYRSPTLV-IAYLM
 GEKV LVHGNAGISRSAAFV-IAYIM
 GSVI LIFSTQGISRSAAAI-IAYLM
 SGKV LVSSEMGISRSAVLV-VAYLM
 GGAC LVYCKNGRSRSAAVC-TAYLM
 NGRV LVHCQAGISRSGTNI-LAYLM
 NHVAA IHCKAGKGRTGVM-IAYLL
 ENIV AIHCKGGTDRTGTMV-CAFLI
 ENIV AIHCKGGKGRTGTMV-CALLI
 ENIV VIHCKGGKGRTGTMV-CACLI
 ENIV VIHCKGGKGRTGTMV-CACLI
 YRKT LIHCYGGGLGRSCLVA-ACLLL
 KSSV LVHCSDGWDRTAQLTSLAMLM
 QRPV LVHCSDGWDRTPOIVALAKLL
 GCCV AVHCVAGLGRAPVLVALA-LI
 GSCV AVHCVAGLGRAPVLVALA-LI
 DKLIG VHCTHGLNRTGYLI-CRYLI
 HKNC VVHCMDGRAASAVAV-CSFLC
 TKSV LFVCLGNICRSPIAEAVFRKL
 EGA IAVHCKAGLGRGTGLI-ACYIM
 RVILI FHCEFSSERGPRMCRFIRER
 HGAT LVHCAAGVSRSATLC-IAYLM
 QGR TLLHCAAGVSRSAALC-LAYLM
 GESCL VHCLAGVSRSVTLV-IAYIM
 DGVV LVHCNAGVSRRAAIV-IGFLM
 GRSV LVHCHAGVSRSAVLI-TAFLM
 GKCV VVHCKAGRSRSATMV-AAYLI
 TGRV LVHCAMGVSRSATLV-LAFLM
 QGL TLLHCMAGVSRASLC-LAYLM
 GGIK LVHCAVGVSRSATLV-LAYLM
 GKGL LIHCQAGVSRSATIV-IAYLM
 GEAV GVHCALGFGRGTML-ACYLV
 HSKCL VHCKMGVSRSASTV-IAYAM
 GSKCL VHCKMGVSRSASTV-IAYAM
 HSKIL VHCVMGSRRSATLV-LAYLM
 GTHV LVHCKMGVSRSAATV-LAYAM
 NGCV LVHCLAGISRSATIA-IAYIM
 GAKV LVHCVGVSRSATLV-LAYLM
 GGNCL VHCFAGISRSSTIV-TAYVM
 -CXXXXXR-

FIG. 7

13/16

*FIG. 8A**FIG. 8B**FIG. 8C**FIG. 8D*

14/16



PTP1B-SO₃ stereo-view of the PTP loop of
PTP1B incubated in pervanadate

FIG. 8E

BEST AVAILABLE COPY

15/16

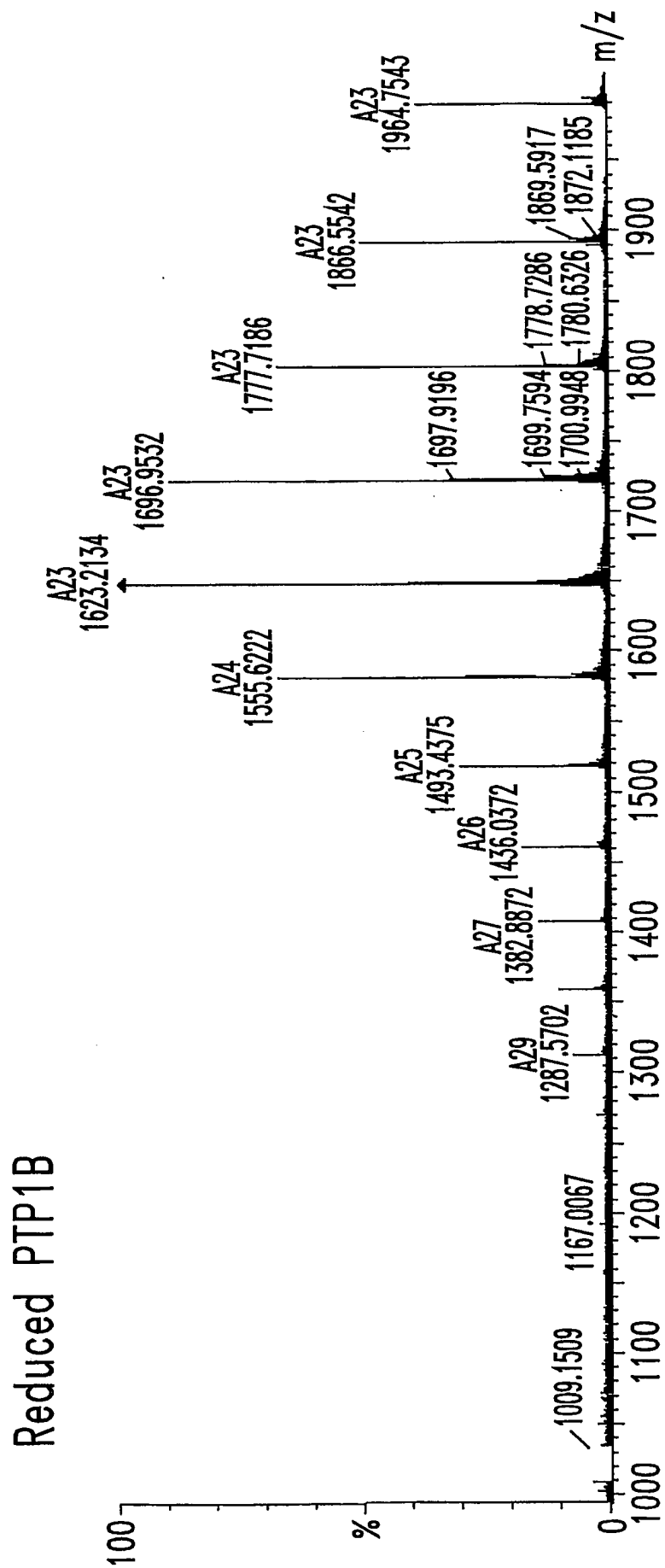


FIG. 9A

Oxidized PTP1B

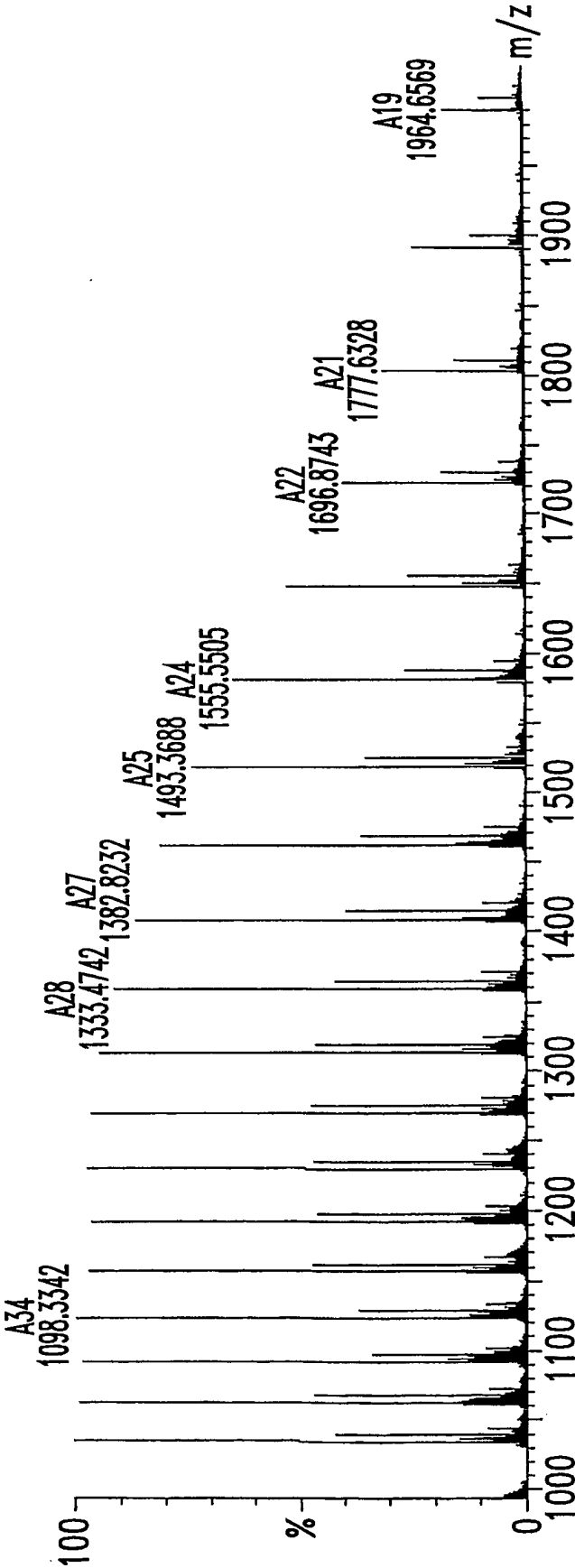


FIG. 9B

SEQUENCE LISTING

<110> Tonks, Nicholas K.
Barford, David
Neel, Benjamin G.
Flint, Andrew J.

<120> NOVEL FORM OF PROTEIN TYROSINE
PHOSPHATASES AND METHODS FOR IDENTIFYING
MOLECULES BINDING THERETO

<130> 200125.450PC

<140> PC

<141> 2004-06-04

<160> 255

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 7

<212> PRT

<213> Unknown

<220>

<223> PTP signature motif

<221> VARIANT

<222> 2, 3, 4, 5, 6

<223> Xaa = Any Amino Acid

<400> 1

Cys Xaa Xaa Xaa Xaa Xaa Arg

1

5

<210> 2

<211> 8

<212> PRT

<213> UNKNOWN

<220>

<223> Catalytic cysteine motif

<221> VARIANT

<222> 3, 4, 5, 6, 7

<223> Xaa = Any Amino Acid

<400> 2

His Cys Xaa Xaa Xaa Xaa Xaa Arg

1

5

<210> 3

<211> 9

<212> PRT

<213> UNKNOWN

<220>

<223> Catalytic cysteine motif

<221> VARIANT

<222> 4, 5, 6, 7, 8

<223> Xaa = Any Amino Acid

<400> 3

Val His Cys Xaa Xaa Xaa Xaa Xaa Arg

1

5

<210> 4

<211> 9

<212> PRT

<213> UNKNOWN

<220>

<223> Catalytic cysteine motif

<221> VARIANT

<222> 4, 5, 6, 7, 8

<223> Xaa = Any Amino Acid

<400> 4

Ile His Cys Xaa Xaa Xaa Xaa Xaa Arg

1

5

<210> 5

<211> 8

<212> PRT

<213> UNKNOWN

<220>

<223> Catalytic cysteine motif

<221> VARIANT

<222> 2, 3, 4, 5, 6

<223> Xaa = Any Amino Acid

<400> 5

Cys Xaa Xaa Xaa Xaa Xaa Arg Ser

1

5

<210> 6

<211> 8

<212> PRT

<213> UNKNOWN

<220>

<223> Catalytic cysteine motif

<221> VARIANT

<222> 2, 3, 4, 5, 6

<223> Xaa = Any Amino Acid

<400> 6

Cys Xaa Xaa Xaa Xaa Xaa Arg Thr

1

5

<210> 7

<211> 9

<212> PRT

<213> UNKNOWN

<220>

<223> Catalytic cysteine motif

<221> VARIANT

<222> 2, 3, 4, 5, 6

<223> Xaa = Any Amino Acid

<400> 7

Cys Xaa Xaa Xaa Xaa Xaa Arg Ser Gly

1

5

<210> 8

<211> 9

<212> PRT

<213> UNKNOWN

<220>

<223> Catalytic cysteine motif

<221> VARIANT

<222> 2, 3, 4, 5, 6

<223> Xaa = Any Amino Acid

<400> 8

Cys Xaa Xaa Xaa Xaa Xaa Arg Thr Gly

1

5

<210> 9

<211> 9

<212> PRT

<213> UNKNOWN

<220>

<223> Catalytic cysteine motif

<221> VARIANT

<222> 3, 4, 5, 6, 7

<223> Xaa = Any Amino Acid

<400> 9

His Cys Xaa Xaa Xaa Xaa Xaa Arg Ser

1

5

<210> 10
<211> 9
<212> PRT
<213> UNKNOWN

<220>
<223> Catalytic cysteine motif

<221> VARIANT
<222> 3, 4, 5, 6, 7
<223> Xaa = Any Amino Acid

<400> 10
His Cys Xaa Xaa Xaa Xaa Xaa Arg Thr
1 5

<210> 11
<211> 10
<212> PRT
<213> UNKNOWN

<220>
<223> Catalytic cysteine motif

<221> VARIANT
<222> 3, 4, 5, 6, 7
<223> Xaa = Any Amino Acid

<400> 11
His Cys Xaa Xaa Xaa Xaa Xaa Arg Ser Gly
1 5 10

<210> 12
<211> 10
<212> PRT
<213> UNKNOWN

<220>
<223> Catalytic cysteine motif

<221> VARIANT
<222> 3, 4, 5, 6, 7
<223> Xaa = Any Amino Acid

<400> 12
His Cys Xaa Xaa Xaa Xaa Xaa Arg Thr Gly
1 5 10

<210> 13
<211> 10
<212> PRT
<213> UNKNOWN

<220>
<223> Catalytic cysteine motif

<221> VARIANT

<222> 4, 5, 6, 7, 8

<223> Xaa = Any Amino Acid

<400> 13

Val His Cys Xaa Xaa Xaa Xaa Arg Ser
1 5 10

<210> 14

<211> 11

<212> PRT

<213> UNKNOWN

<220>

<223> Catalytic cysteine motif

<221> VARIANT

<222> 4, 5, 6, 7, 8

<223> Xaa = Any Amino Acid

<400> 14

Val His Cys Xaa Xaa Xaa Xaa Arg Ser Gly
1 5 10

<210> 15

<211> 10

<212> PRT

<213> UNKNOWN

<220>

<223> Catalytic cysteine motif

<221> VARIANT

<222> 4, 5, 6, 7, 8

<223> Xaa = Any Amino Acid

<400> 15

Val His Cys Xaa Xaa Xaa Xaa Arg Thr
1 5 10

<210> 16

<211> 11

<212> PRT

<213> UNKNOWN

<220>

<223> Catalytic cysteine motif

<221> VARIANT

<222> 4, 5, 6, 7, 8

<223> Xaa = Any Amino Acid

<400> 16

Val His Cys Xaa Xaa Xaa Xaa Arg Thr Gly

1 5 10

<210> 17
<211> 10
<212> PRT
<213> UNKNOWN

<220>
<223> Catalytic cysteine motif

<221> VARIANT
<222> 4, 5, 6, 7, 8
<223> Xaa = Any Amino Acid

<400> 17
Ile His Cys Xaa Xaa Xaa Xaa Xaa Arg Ser
1 5 10

<210> 18
<211> 11
<212> PRT
<213> UNKNOWN

<220>
<223> Catalytic cysteine motif

<221> VARIANT
<222> 4, 5, 6, 7, 8
<223> Xaa = Any Amino Acid

<400> 18
Ile His Cys Xaa Xaa Xaa Xaa Xaa Arg Ser Gly
1 5 10

<210> 19
<211> 10
<212> PRT
<213> UNKNOWN

<220>
<223> Catalytic cysteine motif

<221> VARIANT
<222> 4, 5, 6, 7, 8
<223> Xaa = Any Amino Acid

<400> 19
Ile His Cys Xaa Xaa Xaa Xaa Xaa Arg Thr
1 5 10

<210> 20
<211> 11
<212> PRT
<213> UNKNOWN

<220>

<223> Catalytic cysteine motif

<221> VARIANT

<222> 4, 5, 6, 7, 8

<223> Xaa = Any Amino Acid

<400> 20

Ile His Cys Xaa Xaa Xaa Xaa Xaa Arg Thr Gly
1 5 10

<210> 21

<211> 10

<212> PRT

<213> UNKNOWN

<220>

<223> Motif sequence of "classical" PTPs.

<221> VARIANT

<222> 4, 6, 9

<223> Xaa = Any Amino Acid

<400> 21

His Cys Ser Xaa Gly Xaa Gly Arg Xaa Gly
1 5 10

<210> 22

<211> 4

<212> PRT

<213> Unknown

<220>

<223> Insulin receptor kinase motif.

<221> VARIANT

<222> 1

<223> Xaa = Asp or Glu

<221> VARIANT

<222> 4

<223> Xaa = Arg or Lys

<400> 22

Xaa Tyr Tyr Xaa
1

<210> 23

<211> 3247

<212> DNA

<213> Homo sapiens

<400> 23

gggcgggcct cggggctaag agcgcgacgc ctagagcggc agacggcgca gtgggccgag 60

```

aaggaggcgc agcagccgcc ctggcccgtc atggagatgg aaaaggagtt cgagcagatc 120
gacaagtccg ggagctgggc ggccatttac caggatatcc gacatgaagc cagtgaactc 180
ccatgtagag tggccaagct tccataagaac aaaaaccgaa ataggtacag agacgtcagt 240
ccctttgacc atagtcggat taaactacat caagaagata atgactatat caacgctagt 300
ttgataaaaa tggagaagag ccaaaggagt tacattctta cccagggccc tttgcctaac 360
acatgcggtc acttttggga gatggtgtgg gagcagaaaa gcaggggtgt cgtcatgctc 420
aacagagtga tggagaaagg ttcgtaaata tggcacaat actggccaca aaaagaagaa 480
aaagagatga tctttgaaga cacaatttg aaattaacat tgatctctga agatatcaag 540
tcattataa cagtgcgaca gctagaattg gaaaacctta caaccaaga aactcgagag 600
atcttacatt tccactatac cacatggcct gactttggag tccctgaatc accagcctca 660
ttcttgaact ttcttttcaa agtccgagag tcagggtcac tcagcccga gcacgggccc 720
gttggtgtgc actgcagtgc aggcacggc aggtctggaa ccttctgtct ggctgatacc 780
tgctctctgc tgatggacaa gaggaaagac ccttcttccg ttgatatcaa gaaagtgtct 840
ttagaaatga ggaagtttgc gatgggttg atccagacag ccgaccagct gcgcttctcc 900
tacctggctg tgatcgaagg tgccaaattc atcatggggg actcttccgt gcaggatcag 960
tggaaggagc tttcccacga ggacctggag cccccaccg agcatatccc cccacctccc 1020
cggccaccca aacgaatcct ggagccacac aatgggaaat gcagggagtt cttcccaaat 1080
caccagtggg tgaaggaaga gaccaggag gataaagact gccccatcaa ggaagaaaaa 1140
ggaagccctt taaatgccgc accctacggc atcgaaagca tgagtcaaga cactgaagtt 1200
agaagtcggg tcgtgggggg aagtcttcga ggtgccagg ctgctcccc agccaaaggg 1260
gagccgtcac tgcccagaaa ggacgaggac catgactga gttactggaa gcccttctctg 1320
gtcaacatgt gcgtggctac ggtcctcacg gccggcgctt acctctgcta caggttctctg 1380
ttcaacagca acacatagcc tgacctcct cactccacc tccaccact gtccgcctct 1440
gcccgcagag cccacgcccg actagcaggc atgcccggt aggtaagggc cgccggaccg 1500
cgtagagagc cgggccccgg acggacgttg gttctgcact aaaaccctc tttcccgat 1560
gtgtgtctca cccctcatcc ttttactttt tgccccttcc actttgagta ccaaattccac 1620
aagccatttt ttgaggagag tgaaagagag taccatgctg gcggcgcaga ggggaagggc 1680
ctacaccgtt ctgggggtc gccccacca gggctccctc ctggagcatc ccaggcgccg 1740
cacgccaaca gcccccctt tgaatctgca gggagcaact ctccactcca tatttattta 1800
aacaattttt tccccaaagg catccatagt gactagcat tttcttgaa caataatgta 1860
ttaaaatttt ttgatgtcag ccttgcatac agggctttat caaaaagta aataataaat 1920
cctcaggtag tactgggaat ggaaggcttt gccatgggc tgctgcgtca gaccagtact 1980
gggaaggagg acggttgtaa gcagttgtta tttagtata ttgtgggtaa cgtgagaaga 2040
tagaacaatg ctataatata taatgaacac gtgggtattt aataagaaac atgatgtgag 2100
attactttgt cccgcttatt ctctccctg ttatctgcta gatctagttc tcaatcactg 2160
ctccccctg tgtattagaa tgcatgtaag gtcttctgt gtctgatga aaaatatgtg 2220
cttgaaatga gaaactttga tctctgtta ctaatgtgcc ccatgtccaa gtccaacctg 2280
cctgtgcatg acctgatcat tacatggctg tggttcctaa gcctgttgct gaagtcattg 2340
tcgctcagca atagggtgca gttttccagg aataggcatt tgctaattcc tggcatgaca 2400
ctctagtac ttctgttgga ggcccagcct gtccgtgtac agcagggctc tgctgtaact 2460
cagacattcc aagggtatgg gaagccatat tcacacctca cgctctggac atgatttagg 2520
gaagcaggga cccccccgc cccccacct tgggatcagc ctccgccatt ccaagtcaac 2580
actcttcttg agcagaccgt gatttggag agaggcacct gctggaaacc acacttcttg 2640
aaacagcctg ggtgacggtc ctttaggcag cctgccgccg tctctgtccc ggttcacctt 2700
gccgagagag gcgctgtgc cccacctca aacctgtgg gcctgatgg tgctcacgac 2760
tcttctgca aagggaaact aagacctca cattaagtgg ctttttaaca tgaaaaacac 2820
ggcagctgta gctcccagag tactctcttg ccagcatttt cacattttgc ctttctctg 2880
gtagaagcca gtacagagaa attctgtgtt ggaacattc gaggtgtcac cctgcagagc 2940
tatggtgagg tgtggataag gcttaggtg caggctgtaa gcattctgag ctggcttgtt 3000
gtttttaagt cctgtatatg tatgtagtag tttgggtgtg tatatatagt agcatttcaa 3060
aatggacgta ctggtttaac ctctatcct tggagagcag ctggctctcc acctgtttac 3120
acattatgtt agagaggtag cgagctgtc tgctatatgc ctttaagcaa tatttactca 3180
tcaggtcatt attttttaca atggccatgg aataaaccat ttttacaaaa ataaaaacaa 3240
aaaaagc
3247

```

<210> 24

<211> 435

<212> PRT

<213> Homo sapiens

<400> 24

```

Met Glu Met Glu Lys Glu Phe Glu Gln Ile Asp Lys Ser Gly Ser Trp
 1          5          10          15
Ala Ala Ile Tyr Gln Asp Ile Arg His Glu Ala Ser Asp Phe Pro Cys
 20          25          30
Arg Val Ala Lys Leu Pro Lys Asn Lys Asn Arg Asn Arg Tyr Arg Asp
 35          40          45
Val Ser Pro Phe Asp His Ser Arg Ile Lys Leu His Gln Glu Asp Asn
 50          55          60
Asp Tyr Ile Asn Ala Ser Leu Ile Lys Met Glu Glu Ala Gln Arg Ser
 65          70          75          80
Tyr Ile Leu Thr Gln Gly Pro Leu Pro Asn Thr Cys Gly His Phe Trp
 85          90          95
Glu Met Val Trp Glu Gln Lys Ser Arg Gly Val Val Met Leu Asn Arg
 100          105          110
Val Met Glu Lys Gly Ser Leu Lys Cys Ala Gln Tyr Trp Pro Gln Lys
 115          120          125
Glu Glu Lys Glu Met Ile Phe Glu Asp Thr Asn Leu Lys Leu Thr Leu
 130          135          140
Ile Ser Glu Asp Ile Lys Ser Tyr Tyr Thr Val Arg Gln Leu Glu Leu
 145          150          155          160
Glu Asn Leu Thr Thr Gln Glu Thr Arg Glu Ile Leu His Phe His Tyr
 165          170          175
Thr Thr Trp Pro Asp Phe Gly Val Pro Glu Ser Pro Ala Ser Phe Leu
 180          185          190
Asn Phe Leu Phe Lys Val Arg Glu Ser Gly Ser Leu Ser Pro Glu His
 195          200          205
Gly Pro Val Val Val His Cys Ser Ala Gly Ile Gly Arg Ser Gly Thr
 210          215          220
Phe Cys Leu Ala Asp Thr Cys Leu Leu Leu Met Asp Lys Arg Lys Asp
 225          230          235          240
Pro Ser Ser Val Asp Ile Lys Lys Val Leu Leu Glu Met Arg Lys Phe
 245          250          255
Arg Met Gly Leu Ile Gln Thr Ala Asp Gln Leu Arg Phe Ser Tyr Leu
 260          265          270
Ala Val Ile Glu Gly Ala Lys Phe Ile Met Gly Asp Ser Ser Val Gln
 275          280          285
Asp Gln Trp Lys Glu Leu Ser His Glu Asp Leu Glu Pro Pro Pro Glu
 290          295          300
His Ile Pro Pro Pro Pro Arg Pro Pro Lys Arg Ile Leu Glu Pro His
 305          310          315          320
Asn Gly Lys Cys Arg Glu Phe Phe Pro Asn His Gln Trp Val Lys Glu
 325          330          335
Glu Thr Gln Glu Asp Lys Asp Cys Pro Ile Lys Glu Glu Lys Gly Ser
 340          345          350
Pro Leu Asn Ala Ala Pro Tyr Gly Ile Glu Ser Met Ser Gln Asp Thr
 355          360          365
Glu Val Arg Ser Arg Val Val Gly Gly Ser Leu Arg Gly Ala Gln Ala
 370          375          380
Ala Ser Pro Ala Lys Gly Glu Pro Ser Leu Pro Glu Lys Asp Glu Asp
 385          390          395          400
His Ala Leu Ser Tyr Trp Lys Pro Phe Leu Val Asn Met Cys Val Ala
 405          410          415
Thr Val Leu Thr Ala Gly Ala Tyr Leu Cys Tyr Arg Phe Leu Phe Asn
 420          425          430
Ser Asn Thr

```

435

<210> 25
 <211> 3318
 <212> DNA
 <213> Homo sapiens

<400> 25

```

gtgatgcgta gttccggctg ccggttgaca tgaagaagca gcagcgggcta gggcggcggt 60
agctgcaggg gtcggggatt gcagcgggcc tcgggggctaa gagcgcgacg cggcctagag 120
cggcagacgg cgcagtgggc cgagaaggag gcgcagcagc cgccctggcc cgtcatggag 180
atggaaaagg agttcgagca gatcgacaag tccgggagct gggcggccat ttaccaggat 240
atccgacatg aagccagtga cttcccatgt agagtggcca agcttcctaa gaacaaaaac 300
cgaaataggt acagagacgt cagtcccttt gaccatagtc ggattaaact acatcaagaa 360
gataatgact atatcaacgc tagtttgata aaaatggaag aagcccaaag gagttacatt 420
cttaccaggg gccctttgcc taacacatgc ggtcactttt gggagatggg gtgggagcag 480
aaaagcaggg gtgtcgtcat gctcaacaga gtgatggaga aagggttcgtt aaaatgcgca 540
caatactggc cacaaaaaga agaaaaagag atgatctttg aagacacaaa tttgaaatta 600
acattgatct ctgaagatat caagtcatat tatacagtgc gacagctaga attggaaaac 660
cttacaaccc aagaaactcg agagatctta catttccact ataccacatg gcctgacttt 720
ggagtccctg aatcaccagc ctcatctctg aactttcttt tcaaagtcag agagtcaggg 780
tcaactcagc cggagcacgg gcccgttgtg gtgcactgca gtgcaggcat cggcaggctc 840
ggaaccttct gtctggctga tacctgcctc ttgctgatgg acaagaggaa agacccttct 900
tccgttgata tcaagaaagt gctgttagaa atgaggaagt ttcggatggg gctgatccag 960
acagccgacc agctgcgctt ctccctacct gctgtgatcg aagggtgcaa attcatcatg 1020
ggggactctt ccgtgcagga tcagtggaa gaggctttccc acgaggacct ggagccccc 1080
cccagacata tccccccacc tccccggcca cccaaacgaa tcctggagcc acacaatggg 1140
aaatgcaggg agttcttccc aaatcaccag tgggtgaagg aagagaccca ggaggataaa 1200
gactgcccc tcaaggaaga aaaaggaagc cccttaaag cgcacccta cggcatcgaa 1260
agcatgagtc aagacactga agttagaagt cgggtcgtgg ggggaagtct tcgaggtgcc 1320
caggctgcct cccagcccaa aggggagccg tcactgccc agaggacga ggaccatgca 1380
ctgagttact ggaagccctt cctggtcaac atgtgcgtgg ctacggctct caccggccgc 1440
gcttacctct gctacaggtt cctgttcaac agcaacacat agcctgacct tccctccact 1500
cacctccacc cactgtccgc ctctgcccgc agagcccacg cccgactagc aggcattgcc 1560
cggtaggtaa gggcgcggcg accgcgtaga gagccggggc ccggacggac gttgggttctg 1620
cactaaaacc catcttcccc ggatgtgtgt ctcaacctc atccttttac tttttgcccc 1680
ttccactttg agtaccaaat ccacaagcca ttttttgagg agagtgaag agagtaccat 1740
gctggcggcg cagaggggaag gggcctacac ccgtcttggg gctcgcccca cccagggtc 1800
cctcctggag catcccaggc gggcggcacg ccaacagccc ccccttgaa tctgcaggga 1860
gcaactctcc actccatatt tatttaaaaca attttttccc caaaggcatc catagtgcac 1920
tagcattttc ttgaaccaat aatgtattaa aattttttga tgtcagcctt gcatcaaggg 1980
ctttatcaaa aagtacaata ataaatcctc aggtagtact gggaatggaa ggctttgcca 2040
tgggcctgct gcgtcagacc agtactggga aggaggacgg ttgtaagcag ttgttattta 2100
gtgatattgt gggtaacgtg agaagataga acaatgctat aatatataat gaacacgtgg 2160
gtatttaata agaaacatga tgtgagatta ctttgtcccg ctattctcc tccctgttat 2220
ctgctagatc tagttctcaa tcactgctcc ccggtgtgta ttagaatgca tgaaggtct 2280
tcttgtgtcc tgatgaaaaa tatgtgcttg aaatgagaaa ctttgatctc tgcttactaa 2340
tgtgccccat gtccaagtc aacctgcct tgcataacct gatcattaca tggctgtggg 2400
tcctaaggct gttgctgaag tcattgtcgc tcagcaatag ggtgcagttt tccaggaata 2460
ggcatttgcc taattcctgg catgacactc tagtgacttc ctggtgagc ccagctgtc 2520
ctggtacagc agggctcttc tgtaactcag acattccaag ggtatgggaa gccatattca 2580
cacctcacgc tctggacatg atttaggga gcagggacac ccccgcccc ccaccttg 2640
gatcagcctc cgccattcca agtcaacact cttcttgagc agaccgtgat ttggaagaga 2700
ggcacctgct ggaaccaca cttcttgaaa cagcctgggt gacggctcct taggcagcct 2760
gccgcgctc ctgtcccggt tcaccttgcc gagagaggcg cgtctgcccc acctcaaac 2820
cctgtggggc ctgatgggtc tcacgactct tctgcaaag ggaactgaag acctccacat 2880
taagtggctt ttaacatga aaaacacggc agctgtagct cccgagctac tctcttgcca 2940

```



```

gcattttcac attttgcctt tctcgtggta gaagccagta cagagaaatt ctgtgggtggg 3000
aacattcgag gtgtcaccct gcagagctat ggtgaggtgt ggataaggct taggtgccag 3060
gctgtaagca ttctgagctg ggcttggtgt ttttaagtcc tgtatatgta tgtagtagtt 3120
tggtgtgtgta tatatagtag catttcaaaa tggacgtact ggtttaacct cctatccttg 3180
gagagcagct ggctctccac cttgtttacac attatgttag agaggtagcg agctgctctg 3240
ctatatgcct taagccaata ttactcatc aggtcattat tttttacaat ggccatggaa 3300
taaaccattt ttacaaaa 3318

```

<210> 26

<211> 435

<212> PRT

<213> Homo sapiens

<400> 26

```

Met Glu Met Glu Lys Glu Phe Glu Gln Ile Asp Lys Ser Gly Ser Trp
1 5 10 15
Ala Ala Ile Tyr Gln Asp Ile Arg His Glu Ala Ser Asp Phe Pro Cys
20 25 30
Arg Val Ala Lys Leu Pro Lys Asn Lys Asn Arg Asn Arg Tyr Arg Asp
35 40 45
Val Ser Pro Phe Asp His Ser Arg Ile Lys Leu His Gln Glu Asp Asn
50 55 60
Asp Tyr Ile Asn Ala Ser Leu Ile Lys Met Glu Glu Ala Gln Arg Ser
65 70 75 80
Tyr Ile Leu Thr Gln Gly Pro Leu Pro Asn Thr Cys Gly His Phe Trp
85 90 95
Glu Met Val Trp Glu Gln Lys Ser Arg Gly Val Val Met Leu Asn Arg
100 105 110
Val Met Glu Lys Gly Ser Leu Lys Cys Ala Gln Tyr Trp Pro Gln Lys
115 120 125
Glu Glu Lys Glu Met Ile Phe Glu Asp Thr Asn Leu Lys Leu Thr Leu
130 135 140
Ile Ser Glu Asp Ile Lys Ser Tyr Tyr Thr Val Arg Gln Leu Glu Leu
145 150 155 160
Glu Asn Leu Thr Thr Gln Glu Thr Arg Glu Ile Leu His Phe His Tyr
165 170 175
Thr Thr Trp Pro Asp Phe Gly Val Pro Glu Ser Pro Ala Ser Phe Leu
180 185 190
Asn Phe Leu Phe Lys Val Arg Glu Ser Gly Ser Leu Ser Pro Glu His
195 200 205
Gly Pro Val Val Val His Cys Ser Ala Gly Ile Gly Arg Ser Gly Thr
210 215 220
Phe Cys Leu Ala Asp Thr Cys Leu Leu Leu Met Asp Lys Arg Lys Asp
225 230 235 240
Pro Ser Ser Val Asp Ile Lys Lys Val Leu Leu Glu Met Arg Lys Phe
245 250 255
Arg Met Gly Leu Ile Gln Thr Ala Asp Gln Leu Arg Phe Ser Tyr Leu
260 265 270
Ala Val Ile Glu Gly Ala Lys Phe Ile Met Gly Asp Ser Ser Val Gln
275 280 285
Asp Gln Trp Lys Glu Leu Ser His Glu Asp Leu Glu Pro Pro Pro Glu
290 295 300
His Ile Pro Pro Pro Pro Arg Pro Pro Lys Arg Ile Leu Glu Pro His
305 310 315 320
Asn Gly Lys Cys Arg Glu Phe Phe Pro Asn His Gln Trp Val Lys Glu
325 330 335
Glu Thr Gln Glu Asp Lys Asp Cys Pro Ile Lys Glu Glu Lys Gly Ser
340 345 350

```

Pro	Leu	Asn	Ala	Ala	Pro	Tyr	Gly	Ile	Glu	Ser	Met	Ser	Gln	Asp	Thr
		355					360					365			
Glu	Val	Arg	Ser	Arg	Val	Val	Gly	Gly	Ser	Leu	Arg	Gly	Ala	Gln	Ala
	370					375					380				
Ala	Ser	Pro	Ala	Lys	Gly	Glu	Pro	Ser	Leu	Pro	Glu	Lys	Asp	Glu	Asp
385					390					395					400
His	Ala	Leu	Ser	Tyr	Trp	Lys	Pro	Phe	Leu	Val	Asn	Met	Cys	Val	Ala
			405					410						415	
Thr	Val	Leu	Thr	Ala	Gly	Ala	Tyr	Leu	Cys	Tyr	Arg	Phe	Leu	Phe	Asn
		420						425					430		
Ser	Asn	Thr													
	435														

<210> 27

<211> 2346

<212> DNA

<213> Mus musculus

<400> 27

```

gaattcggga tccttttgca cattcctagtag tagcagtgca tactcatcag actggagatg 60
tttaaatgaca tcaggaacc aaacggacaa cccatagtag ccgaagacag ggtgaaccag 120
acaatcgtaa gcttgatggt gttttccctg actgggtagt tgaagcatct catgaatgtc 180
agccaaattc cgtacagttc ggtgcggatc cgaacgaaac acctcctgta ccagggtccc 240
gtgtcgctct caatttcaat cagctcatct atttgtttgg gagtcttgat tttatttacc 300
gtgaagacct tctctggctg gccccgggct ctcatgttgg tgtcatgaat taacttcaga 360
atcatccagg cttcatcatg ttttcccacc tccagcaaga accgagggct ttctggcatg 420
aaggtgagag ccaccacaga ggagacgcat gggagcgcac agacgatgac gaagacgcgc 480
cacgtgtgga actggttaggc tgaacccatg ctgaagctcc acccgtagtg gggaatgatg 540
gcccaggcat ggcggaggct agatgccgcc aatcatccag aacatgcaga agccgctgct 600
ggggagcttg gggctgcggg ggtggcgggt gacgggcttc gggacgcgga ggcagcgggc 660
ctagcgcggc ggacggccgt gggaactcgg gcagccgacc cgtcccgcca tggagatgga 720
gaaggagttc gaggagatcg acaaggctgg gaactgggcg gctatttacc aggacattcg 780
acatgaagcc agcgacttcc catgcaaagt cgcgaagctt cctaagaaca aaaaccggaa 840
caggtaccga gatgtcagcc cttttgacca cagtcggatt aaattgcacc aggaagataa 900
tgactatatc aatgccagct tgataaaaaat ggaagaagcc cagaggagct atattctcac 960
ccagggccct ttaccaaaaa catgtgggca cttctgggag atgggtgtggg agcagaagag 1020
caggggctgt gtcagtctca accgcatcat ggagaaaggc tcgttaaaat gtgccagta 1080
ttggccacag caagaagaaa aggagatggt ctttgatgac acaggtttga agttgacact 1140
aatctctgaa gatgtcaagt catattacac agtacgacag ttggagttgg aaaacctgac 1200
taccaaggag actcgagaga tcctgcattt ccactacacc acatggcctg actttggagt 1260
ccccgagtca ccggcttctt tcctcaattt ccttttcaaa gtccgagagt caggctcact 1320
cagcctggag catggcccca ttgtgggtcca ctgcagcgcc ggcacgaggc ggtcaggggc 1380
cttctgtctg gctgacacct gcctcttact gatggacaag aggaaagacc catcttccgt 1440
ggacatcaag aaagtactgc tggagatgag caggttccgc atggggctca tccagactgc 1500
cgaccagctg cgcttctcct acctggctgt catcgagggc gccaaagttca tcatgggcga 1560
ctcgtcagtg caggatcagt ggaaggagct ctcccgggag gatctagacc ttccaccgca 1620
gcacgtgccc ccacctcccc ggccacccaa acgcacactg gacctcaca acgggaagtg 1680
caaggagctc ttctccagcc accagtgggt gagcgaggag acctgtgggg atgaagacag 1740
cctggccaga gaggaaggca gagcccagtc aagtgccatg cacagcgtga gcagcatgag 1800
tcagacact gaagttagga gacggatggt ggggtggagg cttcaaagtg ctcaggcgctc 1860
tgtccccacc gaggaagagc tgtcctccac tgaggaggaa cacaaggcac attggccaag 1920
tactggaag ccttccctgg tcaatgtgtg tactggccag ctctggcca ccggcgcgta 1980
cttgtgctac cgggtgtgtt ttacttgaca gactgggagg cactgccact gccagctta 2040
ggatgcggtc tgcggcgtct gacctggtgt agagggaaca acaactcgca agcctgctct 2100
ggaactggaa gggcctgccc caggagggta ttagtgactt gggctttgaa ggagccctg 2160
gtcccacgaa cagagtctaa tctcagggcc ttaacctgtt caggagaagt agaggaaatg 2220
ccaaatactc ttcttgcctc cacctcactc ctccccttct tctgattcat ttgtttttgg 2280

```

```
<210> 28
<211> 432
<212> PRT
<213> Mus musculus
```

<400>	28															
Met	Glu	Met	Glu	Lys	Glu	Phe	Glu	Glu	Ile	Asp	Lys	Ala	Gly	Asn	Trp	
1				5					10					15		
Ala	Ala	Ile	Tyr	Gln	Asp	Ile	Arg	His	Glu	Ala	Ser	Asp	Phe	Pro	Cys	
			20					25					30			
Lys	Val	Ala	Lys	Leu	Pro	Lys	Asn	Lys	Asn	Arg	Asn	Arg	Tyr	Arg	Asp	
		35					40					45				
Val	Ser	Pro	Phe	Asp	His	Ser	Arg	Ile	Lys	Leu	His	Gln	Glu	Asp	Asn	
	50					55					60					
Asp	Tyr	Ile	Asn	Ala	Ser	Leu	Ile	Lys	Met	Glu	Glu	Ala	Gln	Arg	Ser	
65					70					75					80	
Tyr	Ile	Leu	Thr	Gln	Gly	Pro	Leu	Pro	Asn	Thr	Cys	Gly	His	Phe	Trp	
				85					90					95		
Glu	Met	Val	Trp	Glu	Gln	Lys	Ser	Arg	Gly	Val	Val	Met	Leu	Asn	Arg	
			100					105					110			
Ile	Met	Glu	Lys	Gly	Ser	Leu	Lys	Cys	Ala	Gln	Tyr	Trp	Pro	Gln	Gln	
		115					120					125				
Glu	Glu	Lys	Glu	Met	Val	Phe	Asp	Asp	Thr	Gly	Leu	Lys	Leu	Thr	Leu	
	130					135					140					
Ile	Ser	Glu	Asp	Val	Lys	Ser	Tyr	Tyr	Thr	Val	Arg	Gln	Leu	Glu	Leu	
145					150					155					160	
Glu	Asn	Leu	Thr	Thr	Lys	Glu	Thr	Arg	Glu	Ile	Leu	His	Phe	His	Tyr	
				165					170					175		
Thr	Thr	Trp	Pro	Asp	Phe	Gly	Val	Pro	Glu	Ser	Pro	Ala	Ser	Phe	Leu	
			180					185					190			
Asn	Phe	Leu	Phe	Lys	Val	Arg	Glu	Ser	Gly	Ser	Leu	Ser	Leu	Glu	His	
		195					200					205				
Gly	Pro	Ile	Val	Val	His	Cys	Ser	Ala	Gly	Ile	Gly	Arg	Ser	Gly	Thr	
	210					215					220					
Phe	Cys	Leu	Ala	Asp	Thr	Cys	Leu	Leu	Leu	Met	Asp	Lys	Arg	Lys	Asp	
225					230					235					240	
Pro	Ser	Ser	Val	Asp	Ile	Lys	Lys	Val	Leu	Glu	Met	Arg	Arg	Phe		
				245					250					255		
Arg	Met	Gly	Leu	Ile	Gln	Thr	Ala	Asp	Gln	Leu	Arg	Phe	Ser	Tyr	Leu	
			260					265					270			
Ala	Val	Ile	Glu	Gly	Ala	Lys	Phe	Ile	Met	Gly	Asp	Ser	Ser	Val	Gln	
		275					280					285				
Asp	Gln	Trp	Lys	Glu	Leu	Ser	Arg	Glu	Asp	Leu	Asp	Leu	Pro	Pro	Glu	
	290					295					300					
His	Val	Pro	Pro	Pro	Pro	Arg	Pro	Pro	Lys	Arg	Thr	Leu	Glu	Pro	His	
305					310						315				320	
Asn	Gly	Lys	Cys	Lys	Glu	Leu	Phe	Ser	Ser	His	Gln	Trp	Val	Ser	Glu	
				325					330					3		

385		390		395		400
His Trp Pro Ser	His Trp Lys Pro Phe Leu Val Asn Val Cys Met Ala					
	405		410		415	
Thr Leu Leu Ala Thr Gly Ala Tyr Leu Cys Tyr Arg Val Cys Phe His						
	420		425		430	

<210> 29

<211> 3215

<212> DNA

<213> Homo sapiens

<400> 29

```

gcgcgacgcg gcctagagcg gcagacggcg cagtgggccc agaaggaggc gcagcagccg 60
ccctggcccc tcatggagat ggaaaaggag ttcgagcaga tcgacaagtc cgggagctgg 120
gcggccattt accaggatat ccgacatgaa gccagtgact tcccatgtag agtggccaag 180
cttcctaaga acaaaaaccg aaataggtac agagacgtca gtccctttga ccatagtcgg 240
attaaactac atcaagaaga taatgactat atcaacgcta gtttgataaa aatggaagaa 300
gcccaaagga gttacattct taccagggc cctttgccta acacatgcgg tcaacttttg 360
gagatggtgt gggagcagaa aagcaggggt gtcgtcatgc tcaacagagt gatggagaaa 420
ggttcgttaa aatgcgcaca atactggcca caaaaagaag aaaaagagat gatctttgaa 480
gacacaaatt tgaaattaac attgatctct gaagatatca agtcatatta tacagtgcga 540
cagctagaat tggaaaacct tacaacccaa gaaactcgag agatcttaca tttccactat 600
accacatggc ctgacttttg agtccctgaa tcaccagcct cattcttgaa ctttcttttc 660
aaagtccgag agtcagggtc actcagcccg gagcacgggc ccgttgtggg gcaactgcag 720
gcaggcatcg gcaggtcttg aaccttctgt ctggctgata cctgcctctt gctgatggac 780
aagaggaaag acccttcttc cgttgatata aagaaagtgc tgtagaaat gaggaagttt 840
cggatggggc tgatccagac agccgaccag ctgcgcttct cctacctggc tgtgatcgaa 900
ggtgccaaat tcatcatggg ggactcttcc gtgcaggatc agtggaagga gctttccac 960
gaggacctgg agccccacc cgagcatatc ccccccactc cccggccacc caaacgaatc 1020
ctggagccac acaatgggaa atgcaggag ttcttcccaa atcaccagtg ggtgaaggaa 1080
gagaccagg aggataaaga ctgccccatc aaggaagaaa aaggaagccc cttaaagtc 1140
gcacctacg gcatcgaaag catgagtcaa gacactgaag ttagaagtcg ggtcgtggg 1200
ggaagtcttc gaggtgccc ggtgcctcc ccagccaaag gggagccgtc actgcccgag 1260
aaggacgagg accatgcact gagttactgg aagcccttcc tggtaacat gtgcgtggct 1320
acggtctca cgccggcgct ttacctctgc tacaggttcc tgttcaacag caacacatag 1380
cctgacctc ctccactcca cctccacca ctgtccgct ctgcccgcag agcccacgcc 1440
cgactagcag gcatgccggt gtaggtaagg gccgcccggc cgcgtagaga gccgggcccc 1500
ggacggacgt tggttctgca ctaaaaccca tcttccccgg atgtgtgtct caccctcat 1560
ccttttactt tttgccccct ccactttgag taccaaatcc acaagccatt ttttgaggag 1620
agtgaagag agtaccatgc tggcggcgca gaggggaagg gcctacaccc gtcttggggc 1680
tcgccccacc cagggtccc tcctggagca tcccaggcgg gcggcacgcc agacagcccc 1740
ccccttgaat ctgcagggag caactctcca ctccatattt atttaaaca ttttttcccc 1800
aaaggcatcc atagtgcact agcattttct tgaaccaata atgtattaaa attttttgat 1860
gtcagccttg catcaagggc tttatcaaaa agtacaataa taaatcctca ggtagtactg 1920
ggaatggaag gctttgccat gggcctgctg cgtcagacca gtactgggaa ggaggacgg 1980
tgtaagcagt tgttatttag tgatattgtg ggtaacgtga gaagatagaa caatgctata 2040
atatataatg aacacgtggg tatttaataa gaaacatgat gtgagattac tttgtccccg 2100
ttattctgct cctgtttatc tgctagatct agttctcaat cactgctccc ccgtgtgtat 2160
tagaatgcat gtaaggtctt cttgtgtcct gatgaaaaat atgtgcttga aatgagaaaac 2220
tttgatctct gcttactaat gtgccccatg tccaagtcca acctgcctgt gcatgacctg 2280
atcattacat ggctgtgggt cctaagcctg ttgctgaagt cattgtcgct cagcaatagg 2340
gtgcagtttt ccaggaatag gcatttgctt aattcctggc atgacactct agtgacttcc 2400
tggtgaggcc cagcctgtcc tggtagagca gggctcttgc gtaactcaga cattccaagg 2460
gtatgggaag ccatattcac acctcacgct ctggacatga tttagggaag cagggaacac 2520
ccccgcccc cacccttggg atcagcctcc gccattccaa gtcgacactc ttcttgagca 2580
gaccgtgatt tggaagagag gcacctgctg gaaaccacac ttcttgaaac agcctgggtg 2640
acggctcttt aggcagcctg ccgcgctctc tgtcccgtt cacttgccg agagaggcgc 2700

```

```

gtctgcccc  cctcaaaacc  ctgtggggcc  tgatgggtgct  cagcactctt  cctgcaaagg  2760
gaactgaaga  cctccacatt  aagtggcttt  ttaacatgaa  aaacacggca  gctgtagctc  2820
ccgagctact  ctcttgccag  cattttcaca  ttttgctttt  ctctgggtag  aagccagtac  2880
agagaaattc  tgtgggtggg  acattcgagg  tgtcaccttg  cagagctatg  gtgaggtgtg  2940
gataaggctt  aggtgccagg  ctgtaagcat  tctgagctgg  cttgttggtt  ttaagtcttg  3000
tatatgtatg  tagtagtttg  ggtgtgtata  tatagtagca  tttcaaaatg  gacgtactgg  3060
tttaacctcc  tatccttgga  gacgagctgg  ctctccacct  tgttacacat  tatgttagag  3120
aggtagcgag  ctgctctgct  atgtccttaa  gccaatattt  actcatcagg  tcattatttt  3180
ttacaatggc  catggaataa  accattttta  caaaa                      3215

```

<210> 30

<211> 435

<212> PRT

<213> Homo sapiens

<400> 30

```

Met Glu Met Glu Lys Glu Phe Glu Gln Ile Asp Lys Ser Gly Ser Trp
 1              5              10              15
Ala Ala Ile Tyr Gln Asp Ile Arg His Glu Ala Ser Asp Phe Pro Cys
 20              25              30
Arg Val Ala Lys Leu Pro Lys Asn Lys Asn Arg Asn Arg Tyr Arg Asp
 35              40              45
Val Ser Pro Phe Asp His Ser Arg Ile Lys Leu His Gln Glu Asp Asn
 50              55              60
Asp Tyr Ile Asn Ala Ser Leu Ile Lys Met Glu Glu Ala Gln Arg Ser
 65              70              75              80
Tyr Ile Leu Thr Gln Gly Pro Leu Pro Asn Thr Cys Gly His Phe Trp
 85              90              95
Glu Met Val Trp Glu Gln Lys Ser Arg Gly Val Val Met Leu Asn Arg
100              105              110
Val Met Glu Lys Gly Ser Leu Lys Cys Ala Gln Tyr Trp Pro Gln Lys
115              120              125
Glu Glu Lys Glu Met Ile Phe Glu Asp Thr Asn Leu Lys Leu Thr Leu
130              135              140
Ile Ser Glu Asp Ile Lys Ser Tyr Tyr Thr Val Arg Gln Leu Glu Leu
145              150              155              160
Glu Asn Leu Thr Thr Gln Glu Thr Arg Glu Ile Leu His Phe His Tyr
165              170              175
Thr Thr Trp Pro Asp Phe Gly Val Pro Glu Ser Pro Ala Ser Phe Leu
180              185              190
Asn Phe Leu Phe Lys Val Arg Glu Ser Gly Ser Leu Ser Pro Glu His
195              200              205
Gly Pro Val Val Val His Cys Ser Ala Gly Ile Gly Arg Ser Gly Thr
210              215              220
Phe Cys Leu Ala Asp Thr Cys Leu Leu Leu Met Asp Lys Arg Lys Asp
225              230              235              240
Pro Ser Ser Val Asp Ile Lys Lys Val Leu Leu Glu Met Arg Lys Phe
245              250              255
Arg Met Gly Leu Ile Gln Thr Ala Asp Gln Leu Arg Phe Ser Tyr Leu
260              265              270
Ala Val Ile Glu Gly Ala Lys Phe Ile Met Gly Asp Ser Ser Val Gln
275              280              285
Asp Gln Trp Lys Glu Leu Ser His Glu Asp Leu Glu Pro Pro Pro Glu
290              295              300
His Ile Pro Pro Pro Pro Arg Pro Pro Lys Arg Ile Leu Glu Pro His
305              310              315              320
Asn Gly Lys Cys Arg Glu Phe Phe Pro Asn His Gln Trp Val Lys Glu
325              330              335

```

Glu	Thr	Gln	Glu	Asp	Lys	Asp	Cys	Pro	Ile	Lys	Glu	Glu	Lys	Gly	Ser
			340					345					350		
Pro	Leu	Asn	Ala	Ala	Pro	Tyr	Gly	Ile	Glu	Ser	Met	Ser	Gln	Asp	Thr
		355					360					365			
Glu	Val	Arg	Ser	Arg	Val	Val	Gly	Gly	Ser	Leu	Arg	Gly	Ala	Gln	Ala
	370					375					380				
Ala	Ser	Pro	Ala	Lys	Gly	Glu	Pro	Ser	Leu	Pro	Glu	Lys	Asp	Glu	Asp
385					390				395						400
His	Ala	Leu	Ser	Tyr	Trp	Lys	Pro	Phe	Leu	Val	Asn	Met	Cys	Val	Ala
			405					410						415	
Thr	Val	Leu	Thr	Ala	Gly	Ala	Tyr	Leu	Cys	Tyr	Arg	Phe	Leu	Phe	Asn
		420						425					430		
Ser	Asn	Thr													
		435													

<210> 31

<211> 4127

<212> DNA

<213> Rattus norvegicus

<400> 31

```

agccgctgct ggggaggttg gggctgaggt ggtggcgggc gacgggcctc gagacgcgga 60
gcgacgcggc ctacgcgggc ggacggccga gggaaactcg gcagtcgtcc cgtcccgcca 120
tggaaatgga gaaggaattc gagcagatcg ataaggctgg gaactgggcg gctatttacc 180
aggatattcg acatgaagcc agtgacttcc catgcagaat agcgaaactt cctaagaaca 240
aaaaccggaa caggtaccga gatgtcagcc cttttgacca cagtcggatt aaattgcac 300
aggaagataa tgactatatc aatgccagct tgataaaaaat ggaggaagcc cagaggagct 360
atatectcac ccagggccct ttaccaaaca cgtgcgggca cttctgggag atgggtgtgg 420
agcagaagag caggggcgtg gtcagtctca accgcatcat ggagaaaggc tcgttaaaat 480
gtgcccagta ttggccacag aaagaagaaa aagagatggg cttcgatgac accaatttga 540
agctgacact gatctctgaa gatgtcaagt catattacac agtacggcag ttggagttgg 600
agaacctggc taccaggag gctcgagaga tctgcattt ccactacacc acctggcctg 660
actttggagt ccctgagtca cctgcctctt tctcaattt cctattcaaa gtccgagagt 720
caggtcact cagcccagag cacggcccca ttgtggtcca ctgcagtgtt ggcattggca 780
ggtcagggac cttctgctg gctgacacct gcctcttact gatggacaag aggaaagacc 840
cgtcctctgt ggacatcaag aaagtgtgt tggagatgcg caggttccgc atggggctca 900
tccagacggc cgaccaactg cgcttctcct acctggctgt gatcgagggt gcaaagttca 960
tcatgggcga ctcgtcagt caggatcagt ggaaggagct ttcccatgaa gacctggagc 1020
ctccccctga gcacgtgccc ccacctcccc ggccacccaa acgcacattg gagcctcaca 1080
atggcaagtg caaggagctc ttctccaacc accagtgggt gagcgaggag agctgtgagg 1140
atgaggacat cctggccaga gaggaagca gagccccctc aattgctgtg cacagcatga 1200
gcagtatgag tcaagacact gaagttagga aacggatggg gggtaggagt cttcaaagt 1260
ctcaggcatc tgtccccact gaggaagagc tgtccccaac cgaggaggaa caaaaggcac 1320
acaggccagt tcaactggaag cccttccttg tcaacgtgtg catggccacg gccctggcga 1380
ctggcgcgta cctctgttac cgggtatgtt ttactgaca gactgctgtg aggcattgagc 1440
gtggtgggcg ctgccactgc ccagggttagg atttggtctg cggcgtctaa cctgggtgtg 1500
aagaaacaac agcttacaag cctgtggtgg aactggaagg gccagcccca ggaggggcat 1560
ctgtgcactg ggccttgaag gagcccctgg tcccaagaac agagtctaata ctcagggcct 1620
taactgttc aggagaagta gaggaactct caaatactct tcttgctctc acctcactcc 1680
tcccccttct ctggttcgtt tgttttttga aaaaaaaa aaagaattac aacacattgt 1740
tgtttttaac atttataaag gcagggtttt gttattttta gagaaaaaaa aagatgctag 1800
gcactggtga gattctcttg tgcccttttg catgtgatca gattcacgat ttacgtttat 1860
ttccggggga ggggtccacc tgtcaggact gtaaagtcc tgctggcttg gtcagcccc 1920
ccaccccccc accccgagct tgcagggtgcc ctgctgtgag gagagcagca gcagaggctg 1980
cccctggaca gaagcccagc tctgcttccc tcagggtgtc ctgctgttcc atcctcttc 2040
tttgtgaccg ccattcttga gatgaccag tcctcagcac cccacccctg cagatgggtt 2100
tctccgaggg cctgcctcag ggtcatcaga ggttggtctg cagcttagag ctggggcttc 2160

```

```

catttgattg gaaagtcatt actattctat gtagaagcca ctccactgag gtgtaaagca 2220
agactcataa aggaggagcc ttgggtgtcat ggaagtcact ccgcgcgcag gacctgtaac 2280
aacctctgaa acactcagtc ctgctgcagt gacgtccttg aaggcatcag acagatgatt 2340
tgcagactgc caagacttgt cctgagccgt gattttttaga gtctggactc atgaaacacc 2400
gccgagcgct tactgtgcag cctctgatgc tggttggctg aggctgcggg gaggtggaca 2460
ctgtgggtgc atccagtgcg gttgcttttg tgcagttggg tccagcagca cagcccgcac 2520
tccagcctca gctgcaggcc acagtggcca tggaggccgc cagagcgagc tgggggtggat 2580
gcttgttcac ttggagcagc cttcccagga cgtgcagctc ctttcctgct ttgtccttct 2640
gcttccttcc ctggagtagc aagcccacga gcaatcgtga ggggtgtgag ggagctgcag 2700
aggcatcaga gtggcctgca gcggcgtgag gccccttccc ctccgacacc cccctccaga 2760
ggagccgctc cactgttatt tattcacttt gccacagac acccctgagt gagcacaccc 2820
tgaaactgac cgtgtaaggt gtcagcctgc acccaggacc gtcaggtgca gcaccgggtc 2880
agtcctaggg ttgaggtagg actgacacag ccactgtgtg gctggtgctg gggcaggggc 2940
aggagctgag ggtccttagaa gcaatcttca ggaacagaca acagtgggtg catgtaaagt 3000
ccctgtggct actgatgaca tgtgtaggat gaaggctggc ctttctccca tgactttcta 3060
gatcccgctt cccgtctgct ttccctgtga gttagaaaac acacaggctc ctgtcctggt 3120
ggtgccgtgt gcttgacatg ggaaacttag atgacctgct actggcgggc acctcgcat 3180
cgccaccact cagagtgaga gcagtgcgtg ccagtgcgca ggccgcctga ctcccgagc 3240
gactcttcag gctctggcct gccccagcac accccgctgg atctcagaca ttccacaccc 3300
acacctcatt ccctggacac ttgggcaagc agggccgccc ttccacctct ggggtcagcc 3360
cctccattcc gagttcacac tgctctggag caggccagga ccggaagcaa ggcagctggg 3420
gaggagcacc ctccctgggaa cagtgtaggc gacagtctg agagtcagct tgctagcgt 3480
gctggcacca gtcaccttgc tcagaagtgt gtggctcttg aggctgaaga gactgatgat 3540
ggtgctcatg actcttctgt gaggggaact tgaccttcac attgggtggc tttttttaa 3600
ataagcgaag gcagctggaa ctccagtctg cctcttgcca gcacttcaca ttttgcctt 3660
caccagaga agccagcaca gagccactgg ggaaggcgat ggccttgccg gcacaggctg 3720
aggagatggc tcagccggcg tccaggctgt gtctggagca ggggtgcac agcagcctca 3780
caggtggggg cctcagagca ggcgctgccc tgtccctgct cccgctggag gcagcaaagc 3840
tgctgcatgc cttaagtcaa tacttactca gcaggcgct ctggttctct ctctctctct 3900
ctctctctct ctctctctct ctctctctct ctctaaatgg ccatagaata aaccatttta 3960
caaaaataaa agccaacaac aaagtgtctt ggaatagcac ctttgagga gcgggggggtg 4020
tctcaggggc ttctgtgacc tcaccgaact gtccgactgc accgtttcca acttgtgtct 4080
cactaatggg tctgcattag ttgcaacaat aaatgttttt aaagaac 4127

```

<210> 32

<211> 432

<212> PRT

<213> Rattus norvegicus

<400> 32

```

Met Glu Met Glu Lys Glu Phe Glu Gln Ile Asp Lys Ala Gly Asn Trp
 1           5           10          15
Ala Ala Ile Tyr Gln Asp Ile Arg His Glu Ala Ser Asp Phe Pro Cys
 20          25          30
Arg Ile Ala Lys Leu Pro Lys Asn Lys Asn Arg Asn Arg Tyr Arg Asp
 35          40          45
Val Ser Pro Phe Asp His Ser Arg Ile Lys Leu His Gln Glu Asp Asn
 50          55          60
Asp Tyr Ile Asn Ala Ser Leu Ile Lys Met Glu Ala Gln Arg Ser
 65          70          75          80
Tyr Ile Leu Thr Gln Gly Pro Leu Pro Asn Thr Cys Gly His Phe Trp
 85          90          95
Glu Met Val Trp Glu Gln Lys Ser Arg Gly Val Val Met Leu Asn Arg
100          105          110
Ile Met Glu Lys Gly Ser Leu Lys Cys Ala Gln Tyr Trp Pro Gln Lys
115          120          125
Glu Glu Lys Glu Met Val Phe Asp Asp Thr Asn Leu Lys Leu Thr Leu
130          135          140

```

Ile Ser Glu Asp Val Lys Ser Tyr Tyr Thr Val Arg Gln Leu Glu Leu
 145 150 155 160
 Glu Asn Leu Ala Thr Gln Glu Ala Arg Glu Ile Leu His Phe His Tyr
 165 170 175
 Thr Thr Trp Pro Asp Phe Gly Val Pro Glu Ser Pro Ala Ser Phe Leu
 180 185 190
 Asn Phe Leu Phe Lys Val Arg Glu Ser Gly Ser Leu Ser Pro Glu His
 195 200 205
 Gly Pro Ile Val Val His Cys Ser Ala Gly Ile Gly Arg Ser Gly Thr
 210 215 220
 Phe Cys Leu Ala Asp Thr Cys Leu Leu Leu Met Asp Lys Arg Lys Asp
 225 230 235 240
 Pro Ser Ser Val Asp Ile Lys Lys Val Leu Leu Glu Met Arg Arg Phe
 245 250 255
 Arg Met Gly Leu Ile Gln Thr Ala Asp Gln Leu Arg Phe Ser Tyr Leu
 260 265 270
 Ala Val Ile Glu Gly Ala Lys Phe Ile Met Gly Asp Ser Ser Val Gln
 275 280 285
 Asp Gln Trp Lys Glu Leu Ser His Glu Asp Leu Glu Pro Pro Pro Glu
 290 295 300
 His Val Pro Pro Pro Pro Arg Pro Pro Lys Arg Thr Leu Glu Pro His
 305 310 315 320
 Asn Gly Lys Cys Lys Glu Leu Phe Ser Asn His Gln Trp Val Ser Glu
 325 330 335
 Glu Ser Cys Glu Asp Glu Asp Ile Leu Ala Arg Glu Glu Ser Arg Ala
 340 345 350
 Pro Ser Ile Ala Val His Ser Met Ser Ser Met Ser Gln Asp Thr Glu
 355 360 365
 Val Arg Lys Arg Met Val Gly Gly Gly Leu Gln Ser Ala Gln Ala Ser
 370 375 380
 Val Pro Thr Glu Glu Glu Leu Ser Pro Thr Glu Glu Glu Gln Lys Ala
 385 390 395 400
 His Arg Pro Val His Trp Lys Pro Phe Leu Val Asn Val Cys Met Ala
 405 410 415
 Thr Ala Leu Ala Thr Gly Ala Tyr Leu Cys Tyr Arg Val Cys Phe His
 420 425 430

<210> 33

<211> 5376

<212> DNA

<213> Homo sapiens

<400> 33

agccggagct ggagccgagg cggcggcggg acgcggccgg ccggacaaat ttctgtctag 60
 gctgcgga gcgggcgga ggagccggcg cgagcggtt caggaaccca cggcctctgc 120
 gcgtccccgc gacccttctt cgcgccggc gaagacagcc gggcgccccg gagggcgggc 180
 ggcaggcgcc cgggagatgc ggagcctccg ctgcagcgcg atctgcgcga ccagaccggc 240
 cccccgaga ctatagcctt cactttccct cgggtccacca tggagccctt gtgtccactc 300
 ctgctggtgg gtttttagctt gccgctcgcc agggctctca ggggcaacga gaccactgcc 360
 gacagcaacg agacaaccac gacctcaggc cctccggacc cgggcgcctc ccagccgctg 420
 ctggcctggc tgctactgcc gctgctgctc ctctctctcg tgctccttct cggcgctac 480
 ttcttcaggt tcaggaagca gaggaaagct gtggtcagca ccagcgacaa gaagatgcc 540
 aacggaatct tgaggagca agagcagcaa agggtagtc tgctcagcag gtcaccctca 600
 gggcccaaga agtattttcc catccccgtg gagcacctgg agaggagat ccgtatcaga 660
 tccgcgacg actgcaagca gtttcgggag gagttcaact cattgccatc tggacacata 720
 caaggaactt ttgaactggc aaataaagaa gaaaacagag aaaaaaacag atatcccaac 780
 atccttcca atgaccattc tagggtgatt ctgagccaac tggatggaat tccctgttca 840

gactacatca	atgcttccta	catagatggt	tacaaagaga	agaataaatt	catagcagct	900
caaggtccca	aacaggaaac	ggttaacgac	ttctggagaa	tgggtctggga	gcaaaagtct	960
gcgaccatcg	tcatgttaac	aaacttgaaa	gaaaggaaag	aggaaaagtg	ccatcagtac	1020
tggcccgacc	aaggctgctg	gacctatgga	aacatccggg	tgtgctgga	ggactgctg	1080
gttttggtcg	actacaccat	ccggaagttc	tgcatacagc	cacagctccc	cgacggctgc	1140
aaagccccc	ggctgggtctc	acagctgcac	ttcaccagct	ggcccgaactt	cggagtgcct	1200
tttaccccc	ttgggatgct	gaagttcctc	aagaaagtaa	agacgctcaa	ccccgtgcac	1260
gctgggccc	tcgtggtcca	ctgtagcgcg	ggcgtgggce	ggacgggcac	cttcattgtg	1320
atcgatgcc	tgatggccat	gatgcacgcg	gagcagaagg	tggatgtgtt	tgaatttgtg	1380
tctcgaatcc	gtaatcagcg	ccctcagatg	gttcaaacgg	atatgcagta	cacgttcac	1440
taccaagcct	tactcgagta	ctacctctac	ggggacacag	agctggacgt	gtcctccctg	1500
gagaagcacc	tgacagccat	gcacggcacc	accaccact	tcgacaagat	cgggctggag	1560
gaggagtcca	ggaaattgac	aaatgtccgg	atcatgaagg	agaacatgag	gacgggcaac	1620
ttgccggcaa	acatgaagaa	ggccagggtc	atccagatca	tcccgtatga	cttcaaccga	1680
gtgatccttt	ccatgaaaag	gggtcaagaa	tacacagact	acatcaacgc	atccttcata	1740
gacggctacc	gacagaagga	ctatttcac	gccaccagg	ggccactggc	acacacgggt	1800
gaggacttct	ggaggatgat	ctgggaatgg	aaatcccaca	ctatcgtgat	gctgacggag	1860
gtgcaggaga	gagagcagga	taaatgctac	cagtattggc	caaccgaggg	ctcagttact	1920
catggagaaa	taacgattga	gataaagaat	gatacccttt	cagaagccat	cagtatacga	1980
gactttctgg	tcactctcaa	tcagccccag	gcccggcagg	aggagcaggt	ccgagttagt	2040
cgccagtttc	acttccacgg	ctggcctgag	atcgggattc	ccgccgaggg	caaaggcatg	2100
attgacctca	tcgcagccgt	gcagaagcag	cagcagcaga	caggcaacca	ccccatcacc	2160
gtgcactgca	gtgccggagc	tgggcgaaca	ggtacattca	tagccctcag	caacattttg	2220
gagcgagtaa	aagccgaggg	acttttagat	gtatttcaag	ctgtgaagag	tttacgactt	2280
cagagaccac	atatggtgca	aaccctggaa	cagtatgaat	tctgctacaa	agtgggtacaa	2340
gattttattg	atatattttc	tgattatgct	aattttcaaat	gaagattcct	gccttaaaat	2400
attttttaat	ttaatgggtca	gtatattttg	taaaaatcat	gttaattttat	ttcatagttg	2460
acattaatat	cttccctaata	ttctttgtat	atattttgtt	atgccttaaa	ggccacctgc	2520
tatacagttg	ttaaatctta	aatatgcttt	ttaaaaattg	gaataatgta	ttaagggtcaa	2580
ataaatatccc	ataaaatata	tatttctgct	aatattagta	aatatcttaa	tttttcatta	2640
gattcatatc	atttaatttc	acataattca	cacctttaaa	tggtgtaatc	ttaatatgctg	2700
aagtgtgcct	ctgcaagata	ctaacacaaa	gctcatgtta	agaaaacagt	tgaggactca	2760
gaagtcagtt	gaaaatgcac	tttcctaaca	gtgaattcac	aaccctgaac	agcagacttt	2820
ttggaaggca	aactgttcgt	gatggtacaa	tgtaaatggg	gacttctgta	aagttctcag	2880
tttcggtcca	tgtggtttat	ctttacattt	taaagatcaa	agaagtcttt	acaacctgaa	2940
tccaggtcta	aaacacacta	gagtagctgg	tgactataaa	taatatttta	aatgctgtg	3000
tctacaccat	caagactgtg	tctacactat	cttggtgtaa	cgagaagaga	tgtaaatgct	3060
gggtggtccc	gttgaccac	ggcgttgggt	acaacaaaac	cagccatcgg	agttacacc	3120
caaagcacca	tttgctgtcc	agctgctgt	cgtttgccc	agaccacct	cagaaaaaaa	3180
ccagctgcct	ctcccattct	cccctccctg	tctgccacag	cggcctgggc	tggtccagt	3240
ctatgcctgg	aggctcaaca	caaaacttcc	catccaaaca	ttcagatgaa	ctgagcgtct	3300
tacacacgca	gtacagagga	gcacacatta	ggatagaaac	agtagaataa	ccacgggcaa	3360
ttaaacttta	aattttctga	gcagcatttt	ggtattttaa	catttcttgt	aaaaagctga	3420
gacagtttgt	aagaaaagaa	tccttaaaat	ctagatttat	accatttttt	aaagtccac	3480
ctttcaatgt	ttaataaaac	aaaaagagaa	atccttaatc	taaaagctaa	attatttttg	3540
aatggaaata	ctactgagac	cattgacact	ggataacagt	aatgatccca	ttaccagata	3600
agattgactg	acggggaaaa	aaaaaaaaaa	agaatggggt	gtgaatgtac	caacactgaa	3660
tcttacagca	gttatctttc	tatggccatt	aggtacctag	cagatgtgca	caatataaac	3720
aaaaagatat	ctggcctacc	ttactactaa	aagcatttaa	cacgtgcatt	tttggtactt	3780
ttttttttgt	tttctaaaag	ctacataaag	gccttatttg	acattttcac	tgataactga	3840
tcgcacccctc	atgttgagct	gttcgtcccc	tattcttaa	cagtgtgtgc	aaatgcaacc	3900
ccaggacaca	ttattgttct	gatagatgct	cacagggaa	caagcttctc	gcccactcca	3960
cggctctgag	ccccatccaa	gggcaagact	tggtgcccag	ctggaaggac	gaaagcacac	4020
tttgtgaccg	ccatcctcac	cagctgcatg	cctgggctgc	acactgctga	acgtgctcct	4080
ctctccttct	ctgtacaatg	attcagcatc	tcggcggaag	aggaaaatgg	agctttttga	4140
ggctcgccag	gtcccttttg	ttttcaccat	taaaattcca	aacccaaagc	ctttgtttga	4200
ctgaaggaga	agagagggaa	gtaagcttct	gttcagcacc	tgaaccctag	aaaaagagcc	4260
agtttgctac	gatgaagggtg	acatttctct	ggtcatttat	ttgagagttc	gaagtcaaag	4320

```

tcgaggggca cgggctttgg ttcattgtcta ggagccctct gtcagaatcc ttgaagccct 4380
ttaatggtct aactggcatc tcttgatatca agaagtacct ttaaggtaga ccttttcagg 4440
gtgccctcag gaaagggccc tgctcatgtt tttttcctgt ccccttagac caaccccagg 4500
tgtccactgc aggggttctg cctgttccca aactttttcc attccaggaa caaaggagaa 4560
gccactttcc ccaggacgca agactctccc ctccactgtc cgggacagcg ttcgcccttt 4620
agcggggagg tcattacagc ctcatggcct ctaccaaggc cccagatcac aggatctcct 4680
gggccttgga gcacctcacg ctgggggaat caatccctga gggactcaga atcttctccg 4740
tgcaacctgg aaagttcac tcttgtttcc ttcagtcaaa gaaagtccat tgtacataac 4800
aaaacagccc ccaaacagcc cagtgccgac accattgttc ctttcacact ttcctttgtt 4860
gcatgcagtt gggttcaa at gccaaatagt gattagaaga cgaccattct gatctgtgtg 4920
tgatctggtc actatgtgac tgccctttac gtttctctcc atgtgctata tgaatgaaga 4980
atgcatacca gtgttttaaa aggtatTTTT atgtgttttt aaacactttt ttaa atgagc 5040
ctgacacctg tgtttcagca tttggagaca tccccatgtt attcttttaa gtgtataatt 5100
actgatactt ttttgtttgt ttgtttaact aagttgtgtt taacttatgt gcagctctta 5160
taatgtatgt atgttattac agtttcaact atcatatttt ctttgattac atttataatt 5220
tgatcttgc ctgattataa tgccagtga tggtgctgaa ctctttgtat atgcaaattg 5280
caagatttaa accattctga tgcaaggata aacctttact ttgactacca gcctgtgttt 5340
ttgtctttaa atctctta ttcattcctc tgcaaa 5376

```

<210> 34
 <211> 697
 <212> PRT
 <213> Homo sapiens

<400> 34

```

Met Glu Pro Leu Cys Pro Leu Leu Leu Val Gly Phe Ser Leu Pro Leu
1      5      10      15
Ala Arg Ala Leu Arg Gly Asn Glu Thr Thr Ala Asp Ser Asn Glu Thr
20     25     30
Thr Thr Thr Ser Gly Pro Pro Asp Pro Gly Ala Ser Gln Pro Leu Leu
35     40     45
Ala Trp Leu Leu Leu Pro Leu Leu Leu Leu Leu Leu Val Leu Leu Leu
50     55     60
Ala Ala Tyr Phe Phe Arg Phe Arg Lys Gln Arg Lys Ala Val Val Ser
65     70     75     80
Thr Ser Asp Lys Lys Met Pro Asn Gly Ile Leu Glu Glu Gln Glu Gln
85     90     95
Gln Arg Val Met Leu Leu Ser Arg Ser Pro Ser Gly Pro Lys Lys Tyr
100    105    110
Phe Pro Ile Pro Val Glu His Leu Glu Glu Glu Ile Arg Ile Arg Ser
115    120    125
Ala Asp Asp Cys Lys Gln Phe Arg Glu Glu Phe Asn Ser Leu Pro Ser
130    135    140
Gly His Ile Gln Gly Thr Phe Glu Leu Ala Asn Lys Glu Glu Asn Arg
145    150    155    160
Glu Lys Asn Arg Tyr Pro Asn Ile Leu Pro Asn Asp His Ser Arg Val
165    170    175
Ile Leu Ser Gln Leu Asp Gly Ile Pro Cys Ser Asp Tyr Ile Asn Ala
180    185    190
Ser Tyr Ile Asp Gly Tyr Lys Glu Lys Asn Lys Phe Ile Ala Ala Gln
195    200    205
Gly Pro Lys Gln Glu Thr Val Asn Asp Phe Trp Arg Met Val Trp Glu
210    215    220
Gln Lys Ser Ala Thr Ile Val Met Leu Thr Asn Leu Lys Glu Arg Lys
225    230    235    240
Glu Glu Lys Cys His Gln Tyr Trp Pro Asp Gln Gly Cys Trp Thr Tyr

```

															245																250																255	
Gly	Asn	Ile	Arg	Val	Cys	Val	Glu	Asp	Cys	Val	Val	Leu	Val	Asp	Tyr																																	
															260																265																270	
Thr	Ile	Arg	Lys	Phe	Cys	Ile	Gln	Pro	Gln	Leu	Pro	Asp	Gly	Cys	Lys																																	
															275																280																285	
Ala	Pro	Arg	Leu	Val	Ser	Gln	Leu	His	Phe	Thr	Ser	Trp	Pro	Asp	Phe																																	
															290																295																300	
Gly	Val	Pro	Phe	Thr	Pro	Ile	Gly	Met	Leu	Lys	Phe	Leu	Lys	Lys	Val																																	
305																310																315																320
Lys	Thr	Leu	Asn	Pro	Val	His	Ala	Gly	Pro	Ile	Val	Val	His	Cys	Ser																																	
															325																330																335	
Ala	Gly	Val	Gly	Arg	Thr	Gly	Thr	Phe	Ile	Val	Ile	Asp	Ala	Met	Met																																	
															340																345																350	
Ala	Met	Met	His	Ala	Glu	Gln	Lys	Val	Asp	Val	Phe	Glu	Phe	Val	Ser																																	
															355																360																365	
Arg	Ile	Arg	Asn	Gln	Arg	Pro	Gln	Met	Val	Gln	Thr	Asp	Met	Gln	Tyr																																	
															370																375																380	
Thr	Phe	Ile	Tyr	Gln	Ala	Leu	Leu	Glu	Tyr	Tyr	Leu	Tyr	Gly	Asp	Thr																																	
385																390																395																400
Glu	Leu	Asp	Val	Ser	Ser	Leu	Glu	Lys	His	Leu	Gln	Thr	Met	His	Gly																																	
															405																410																415	
Thr	Thr	Thr	His	Phe	Asp	Lys	Ile	Gly	Leu	Glu	Glu	Glu	Phe	Arg	Lys																																	
															420																425																430	
Leu	Thr	Asn	Val	Arg	Ile	Met	Lys	Glu	Asn	Met	Arg	Thr	Gly	Asn	Leu																																	
															435																440																445	
Pro	Ala	Asn	Met	Lys	Lys	Ala	Arg	Val	Ile	Gln	Ile	Ile	Pro	Tyr	Asp																																	
															450																455																460	
Phe	Asn	Arg	Val	Ile	Leu	Ser	Met	Lys	Arg	Gly	Gln	Glu	Tyr	Thr	Asp																																	
465																470																475																480
Tyr	Ile	Asn	Ala	Ser	Phe	Ile	Asp	Gly	Tyr	Arg	Gln	Lys	Asp	Tyr	Phe																																	
															485																490																495	
Ile	Ala	Thr	Gln	Gly	Pro	Leu	Ala	His	Thr	Val	Glu	Asp	Phe	Trp	Arg																																	
															500																505																510	
Met	Ile	Trp	Glu	Trp	Lys	Ser	His	Thr	Ile	Val	Met	Leu	Thr	Glu	Val																																	
															515																520																525	
Gln	Glu	Arg	Glu	Gln	Asp	Lys	Cys	Tyr	Gln	Tyr	Trp	Pro	Thr	Glu	Gly																																	
															530																535																540	
Ser	Val	Thr	His	Gly	Glu	Ile	Thr	Ile	Glu	Ile	Lys	Asn	Asp	Thr	Leu																																	
545																550																555																560
Ser	Glu	Ala	Ile	Ser	Ile	Arg	Asp	Phe	Leu	Val	Thr	Leu	Asn	Gln	Pro																																	
															565																570																575	
Gln	Ala	Arg	Gln	Glu	Gln	Val	Arg	Val	Val	Arg	Gln	Phe	His	Phe																																		
															580																585																590	
His	Gly	Trp	Pro	Glu	Ile	Gly	Ile	Pro	Ala	Glu	Gly	Lys	Gly	Met	Ile																																	
															595																600																605	
Asp	Leu	Ile	Ala	Ala	Val	Gln	Lys	Gln	Gln	Gln	Gln	Thr	Gly	Asn	His																																	
															610																615																620	
Pro	Ile	Thr	Val	His	Cys	Ser	Ala	Gly	Ala	Gly	Arg	Thr	Gly	Thr	Phe																																	
625																630																635																640
Ile	Ala	Leu	Ser	Asn	Ile	Leu	Glu	Arg	Val	Lys	Ala	Glu	Gly</																																			

<210> 35
 <211> 5002
 <212> DNA
 <213> Homo sapiens

<400> 35

```

gtgcagcaga gggcagctga gaggctgggt ggctgggcct gggagacaca cagaggccag 60
gccttagcgc ggctcagcca tgagcaacag gagtagcttt tcccgggtca cctgggttcag 120
gaagcagagg aaagctgtgg tcagcaccag cgacaagaag atgcccacag gaatcttggg 180
ggagcaagag cagcaaaggg tgatgctgct cagcagggtca ccctcagggc ccaagaagta 240
ttttcccatc cccgtggagc acctggagga ggagatccgt atcagatccg ccgacgactg 300
caagcagttt cgggaggagt tcaactcatt gccatctgga cacatacaag gaacttttga 360
actggcaaat aaagaagaaa acagagaaaa aaacagatat cccaacatcc ttcccaatga 420
ccattctagg gtgattctga gccactgga tgggaattccc tggttcagact acatcaatgc 480
ttcctacata gatggttaca aagagaagaa taaattcata gcagctcaag gtcccaaaaca 540
ggaaacgggt aacgacttct ggagaatggt ctgggagcaa aagtctgcca ccctcgcat 600
gttaacaaac ttgaaagaaa ggaaagagga aaagtgccat cagtactggc ccgaccaagg 660
ctgctggacc tatggaaaca tccgggtgtg cgtggaggac tgctgtggtt tggtcgacta 720
caccatccgg aagtcttgca tacagccaca gctccccgac ggctgcaaag ccccagggt 780
ggtctcacag ctgcacttca ccagctggcc cgacttcgga gtgcctttta ccccattgg 840
gatgctgaag ttctcaaga aagtaaagac gctcaacccc gtgcacgctg ggcccatcgt 900
ggtccactgt agcgcgggcg tgggccggac gggcaccttc attgtgatcg atgccatgat 960
ggccatgatg cacgcggagc agaaggtgga tgtgtttgaa tttgtgtctc gaatccgtaa 1020
tcagcgccct cagatggttc aaacggatat gcagtacacg ttcactctacc aagccttact 1080
cgagtactac ctctacgggg acacagagct ggacgtgtcc tccctggaga agcacctgca 1140
gaccatgcac ggcaccacca cccacttcga caagatcggg ctggaggagg agttcaggaa 1200
attgacaaat gtccggatca tgaaggagaa catgaggacg ggcaacttgc cggcaaacat 1260
gaagaaggcc agggatcatc agatcatccc gtatgacttc aaccgagtga tcctttccat 1320
gaaaaggggt caagaatata cagactacat caacgcaccc ttcatagacg gctaccgaca 1380
gaaggactat ttcatcgcca ccagggggcc actggcacac acggttgagg acttctggag 1440
gatgatctgg gaattgaaat cccacactat cgtgatgctg acggaggtgc aggagagaga 1500
gcaggataaa tgctaccagt attggccaac cgagggtcga gttactcatg gagaaataac 1560
gattgagata aagaatgata ccctttcaga agccatcagt atacgagact ttctggtcac 1620
tctcaatcag ccccaggccc gccaggagga gcaggtcgga gtagtgcgcc agtttcactt 1680
ccacggctgg cctgagatcg ggattccgcg cgaggggcaa ggcatgattg acctcatcgc 1740
agccgtgcag aagcagcagc agcagacagg caaccacccc atcacctgc actgcagtgc 1800
cggagctggg cgaacaggta cattcatagc cctcagcaac attttggagc gagtaaaagc 1860
cgagggactt ttagatgtat ttcaagctgt gaagagttaa cgacttcaga gaccacatat 1920
ggtgcaaacc ctggaacagt atgaattctg ctacaaagtg gtacaagatt ttattgatat 1980
attttctgat tatgctaatt tcaaatgaag attcctgcct taaaatattt ttttaatttaa 2040
tggtcagtat attttgtaaa aatcatgtta atttatttca tagttgacat taatatcttc 2100
cctaatttct ttgtatatat tttgttatgc cttaaaggcc acctgctata cagttgttaa 2160
atcttaataa tgctttttta aaattggaat aatgtattaa ggtcaaataa tatcccataa 2220
aatatatatt tctgctaata ttagtaaata tcttaatttt tcattagatt catatcattt 2280
aatttcacat attcaacacc tttaaatgtt gtaatcttaa tatgcgaagt gtgcctctgc 2340
aagatactaa cacaagctc atgttaagaa aacagttgag gactcagaag tcagttgaaa 2400
atgcactttc ctaacagtga attcacaacc ctgaacagca gcatttttgg aaggcaaact 2460
gttcgtgatg gtacaatgta aatggggact tctgtaaagt tctcagtttc ggtccatgtg 2520
gtttatcttt acatttttaa gatcaaagaa gtctttacaa cctgaatcca ggtctaaaac 2580
acactagagt agctggtgac tataaataat attttaaaat gctgtgtcta caccatcaag 2640
actgtgtcta cactatcttg gctgaacgag aagagatgta aatgctgggt ggtcccgttg 2700
accacggcgt ttgggtacaa caaaaccagc catcggagtt acaccccaaa gcaccatttg 2760
ctgtccagct gcctgtcggt tggcccagac caccctcaga aaaaaaccag ctgcctctcc 2820
cattctcccc tcccgttctg ccacagcggc ctgggctggt ccagtgtctat gcctggaggc 2880
tcaacacaaa acttcccatc caaacattca gatgaactga gcgtcttaca cacgcagtac 2940
agaggagcac acattaggat agaaacagta gaataaccac gggcaattaa actttaaatt 3000
ttctgagcag catttttgga tttaaacatt tcttgtaaaa agctgagaca gtttgtaaga 3060

```

```

aaagaatcct taaaatctag atttatacca ttttttaaag tcccaccttt caatgttttaa 3120
taaaacaaaa agagaaatcc ttaatctaaa agctaaatta tttttgaatg gaaatactac 3180
tgagaccatt gacactggat aacagtaatg atcccattac cagataagat tgactgacgg 3240
ggaaaaaaaa aaaaaaagaa tggggtgtga atgtaccaac actgaatctt acagcagtta 3300
tctttctatg gccattaggt acctagcaga tgtgcacaat ataaacaaaa agatatctgg 3360
cctaccttac tactaaaagc atttaacacg tgcatttttg gtactttttt ttttgttttc 3420
taaaagctac ataaaggcct tatttgacat tttcactgat aactgatcgc accctcatgt 3480
tgcagtgttc gtcccttatt cattaacagt gtgtgcaaag gcaaccccag gacacattat 3540
tgttctgata gatgtccaca gggaatcaag cttctcgcgc actccacggc tctgagcccc 3600
atccaagggc aagacttggg gccagctgg aaggacgaaa gcacactttg tgaccgccat 3660
ctcaccagc tgcatgcctg ggctgcacac tgcagaacgt gctcctctct ccttctctgt 3720
acaatgattc agcatctcgg cggaagagga aaatggagct ttttgaggct cgccagggtcc 3780
cttttgtttt caccattaaa attccaaacc caaagccttt gtttgactga aggagaagag 3840
agggaaagtaa gcttctgttc agcacctgaa ccctagaaaa agagccagtt tgctacgatg 3900
aaggtgacat ttctctgggc atttatttga gagttcgaag tcaaagtcga ggggcaccgg 3960
ctttggttca tgtctaggag ccctctgtca gaatccttga agccctttta tgggtctaact 4020
ggcatctctt gtatcaagaa gtacctttta ggtagacctt ttcagggtgc cctcaggaaa 4080
gggcctgtct catgtttttt tctgtcccc ttagaccaac cccagggtgc cactgcaggg 4140
gttctgcctg ttcccaaact ttttccattc caggaacaaa ggagaagcca ctttccccag 4200
gacgcaagac tctccctctc actgtccggg acagcgttcg cccttttagcg gggagggtcat 4260
tacagcctca tggcctctac caaggcccca gatcacagga tctcctgggc cttggagcac 4320
ctcacgtgg gggaatcaat ccctgaggga ctcagaatct tctccgtgca acctggaaag 4380
ttcatctctt gtttccttca gtcaaagaaa gtccattgta cataacaaaa cagcccccaa 4440
acagcccagt gccgacacca ttgttccttt cacactttcc tttgttgcat gcagttgggt 4500
tcaaagcca aatagtgatt agaagacgac cattctgatc tgtgtgtgat ctggtcacta 4560
tgtgactgcc tttacggttt ctctccatgt gctatatgaa tgaagaatgc ataccagtgt 4620
tttaaaagggt atttttatgt gtttttaaac acttttttaa atgagcctga cacctgtgtt 4680
tcagcatttg gagacatccc catgttattc ttttaagtgt ataattactg atactttttt 4740
gtttgtttgt ttaactaagt tgtgtttaac ttatgtgcag tctttataat gtatgtatgt 4800
tattacagtt tcaactatca tattttcttt gattacattt ataatttgat cttgctctga 4860
ttataatgcc agtgaatgtt gctgaactct ttgtatatgc aaattgcaag atttaaacca 4920
ttctgatgca aggataaacc tttactttga ctaccagcct gtgtttttgt ctttaaatct 4980
cttaatttca ttcctctgca aa                                     5002

```

<210> 36

<211> 642

<212> PRT

<213> Homo sapiens

<400> 36

```

Met Ser Asn Arg Ser Ser Phe Ser Arg Leu Thr Trp Phe Arg Lys Gln
 1             5             10             15
Arg Lys Ala Val Val Ser Thr Ser Asp Lys Lys Met Pro Asn Gly Ile
      20             25             30
Leu Glu Glu Gln Glu Gln Arg Val Met Leu Leu Ser Arg Ser Pro
      35             40             45
Ser Gly Pro Lys Lys Tyr Phe Pro Ile Pro Val Glu His Leu Glu Glu
      50             55             60
Glu Ile Arg Ile Arg Ser Ala Asp Asp Cys Lys Gln Phe Arg Glu Glu
      65             70             75             80
Phe Asn Ser Leu Pro Ser Gly His Ile Gln Gly Thr Phe Glu Leu Ala
      85             90             95
Asn Lys Glu Glu Asn Arg Glu Lys Asn Arg Tyr Pro Asn Ile Leu Pro
      100            105            110
Asn Asp His Ser Arg Val Ile Leu Ser Gln Leu Asp Gly Ile Pro Cys
      115            120            125

```

Ser	Asp	Tyr	Ile	Asn	Ala	Ser	Tyr	Ile	Asp	Gly	Tyr	Lys	Glu	Lys	Asn
130						135					140				
Lys	Phe	Ile	Ala	Ala	Gln	Gly	Pro	Lys	Gln	Glu	Thr	Val	Asn	Asp	Phe
145					150					155					160
Trp	Arg	Met	Val	Trp	Glu	Gln	Lys	Ser	Ala	Thr	Ile	Val	Met	Leu	Thr
				165					170					175	
Asn	Leu	Lys	Glu	Arg	Lys	Glu	Glu	Lys	Cys	His	Gln	Tyr	Trp	Pro	Asp
			180					185					190		
Gln	Gly	Cys	Trp	Thr	Tyr	Gly	Asn	Ile	Arg	Val	Cys	Val	Glu	Asp	Cys
		195					200					205			
Val	Val	Leu	Val	Asp	Tyr	Thr	Ile	Arg	Lys	Phe	Cys	Ile	Gln	Pro	Gln
	210					215					220				
Leu	Pro	Asp	Gly	Cys	Lys	Ala	Pro	Arg	Leu	Val	Ser	Gln	Leu	His	Phe
225					230					235					240
Thr	Ser	Trp	Pro	Asp	Phe	Gly	Val	Pro	Phe	Thr	Pro	Ile	Gly	Met	Leu
				245					250					255	
Lys	Phe	Leu	Lys	Lys	Val	Lys	Thr	Leu	Asn	Pro	Val	His	Ala	Gly	Pro
		260						265					270		
Ile	Val	Val	His	Cys	Ser	Ala	Gly	Val	Gly	Arg	Thr	Gly	Thr	Phe	Ile
	275						280					285			
Val	Ile	Asp	Ala	Met	Met	Ala	Met	Met	His	Ala	Glu	Gln	Lys	Val	Asp
	290					295					300				
Val	Phe	Glu	Phe	Val	Ser	Arg	Ile	Arg	Asn	Gln	Arg	Pro	Gln	Met	Val
305					310					315					320
Gln	Thr	Asp	Met	Gln	Tyr	Thr	Phe	Ile	Tyr	Gln	Ala	Leu	Leu	Glu	Tyr
				325					330					335	
Tyr	Leu	Tyr	Gly	Asp	Thr	Glu	Leu	Asp	Val	Ser	Ser	Leu	Glu	Lys	His
		340						345					350		
Leu	Gln	Thr	Met	His	Gly	Thr	Thr	Thr	His	Phe	Asp	Lys	Ile	Gly	Leu
	355					360						365			
Glu	Glu	Glu	Phe	Arg	Lys	Leu	Thr	Asn	Val	Arg	Ile	Met	Lys	Glu	Asn
	370					375					380				
Met	Arg	Thr	Gly	Asn	Leu	Pro	Ala	Asn	Met	Lys	Lys	Ala	Arg	Val	Ile
385					390					395					400
Gln	Ile	Ile	Pro	Tyr	Asp	Phe	Asn	Arg	Val	Ile	Leu	Ser	Met	Lys	Arg
				405					410					415	
Gly	Gln	Glu	Tyr	Thr	Asp	Tyr	Ile	Asn	Ala	Ser	Phe	Ile	Asp	Gly	Tyr
			420					425					430		
Arg	Gln	Lys	Asp	Tyr	Phe	Ile	Ala	Thr	Gln	Gly	Pro	Leu	Ala	His	Thr
	435						440					445			
Val	Glu	Asp	Phe	Trp	Arg	Met	Ile	Trp	Glu	Trp	Lys	Ser	His	Thr	Ile
	450					455					460				
Val	Met	Leu	Thr	Glu	Val	Gln	Glu	Arg	Glu	Gln	Asp	Lys	Cys	Tyr	Gln
465					470					475					480
Tyr	Trp	Pro	Thr	Glu	Gly	Ser	Val	Thr	His	Gly	Glu	Ile	Thr	Ile	Glu
				485					490					495	
Ile	Lys	Asn	Asp	Thr	Leu	Ser	Glu	Ala	Ile	Ser	Ile	Arg	Asp	Phe	Leu
		500						505					510		
Val	Thr	Leu	Asn	Gln	Pro	Gln	Ala	Arg	Gln	Glu	Glu	Gln	Val	Arg	Val
	515						520					525			
Val	Arg	Gln	Phe	His	Phe	His	Gly	Trp	Pro	Glu	Ile	Gly	Ile	Pro	Ala
	530					535						540			
Glu	Gly	Lys	Gly	Met	Ile	Asp	Leu	Ile	Ala	Ala	Val	Gln	Lys	Gln	Gln
545					550					555					560
Gln	Gln	Thr	Gly	Asn	His	Pro	Ile	Thr	Val	His	Cys	Ser	Ala	Gly	Ala
				565					570					575	
Gly	Arg	Thr	Gly	Thr	Phe	Ile	Ala	Leu	Ser	Asn	Ile	Leu	Glu	Arg	Val
			580					585					590		

Lys Ala Glu Gly Leu Leu Asp Val Phe Gln Ala Val Lys Ser Leu Arg
 595 600 605
 Leu Gln Arg Pro His Met Val Gln Thr Leu Glu Gln Tyr Glu Phe Cys
 610 615 620
 Tyr Lys Val Val Gln Asp Phe Ile Asp Ile Phe Ser Asp Tyr Ala Asn
 625 630 635 640
 Phe Lys

<210> 37

<211> 5117

<212> DNA

<213> Homo sapiens

<400> 37

```

ccccagccgc atgacgcgcg gaggaggcag cgggacgagc gcgggagccg ggaccgggta 60
gccgcgcgct ggggggtgggc gccgctcgct ccgccccgcg aagcccctgc gcgctcaggg 120
acgcggcccc cccgcggcag ccgcgctagg ctccggcgctg tggccgcggc cgccgcgcgc 180
ctgccatgtc tccgggcaag ccggggcggg cggagcgggg acgaggcgga cgggctggcg 240
gaggaggagg cgaaggagac ggcaggaggc ggcgacgacg gtgcccgggc tcgggcgcac 300
ggcggggccc gattcgcgcg tccggggcac gttccagggc gcgcggggca tgaagccggc 360
ggcgcgggag gcgcggctgc ctccgcgctc gcccgggctg cgctgggcgc tgcgctgct 420
gctgctgctg ctgcgcctgg gccagatcct gtgcgcgagg ggcaccccta gtccaattcc 480
tgacccttca gtagcaactg ttgccacagg ggaaaatggc ataacgcaga tcagcagtac 540
agcagaatcc tttcataaac agaatggaac tggaacacct caggtggaaa caaacaccag 600
tgaggatggt gaaagctctg gagccaacga tagtttaaga acacctgaac aaggatctaa 660
tgggactgat ggggcatctc aaaaaactcc cagtagcact gggcccagtc ctgtgtttga 720
cattaaagct gtttccatca gtccaaccaa tgtgatctta acttgaaaaa gtaatgacac 780
agctgcttct gagtacaagt atgtagtaaa gcataagatg gaaaatgaga agacaattac 840
tggtgtgcat caaccatggt gtaacatcac aggcttacgt ccagcgactt catatgtatt 900
ctccatcact ccaggaatag gcaatgagac ttggggagat cccagagtca taaaagtcac 960
cacagagccg atcccagttt ctgatctccg tgttgccctc acgggtgtga ggaaggctgc 1020
tctctcctgg agcaatggca atggcacccg ctccctgcgg gttcttcttg aaagcattgg 1080
aagccatgag gagttgactc aagactcaag acttcaggtc aatatctcgg acctgaagcc 1140
aggggttcaa tacaacatca acccgatatc tctacaatca aataagacaa agggagaccc 1200
cttgggcaca gaagggtggct tggatgccag caatacagag agaagccggg caggagaccc 1260
caccgccccct gtgcatgatg agtccctcgt gggacctgtg gacctatcct ccggccagca 1320
gtcccagacac acggaagtcc tgcctgtcgg gttagagcct ggcacccgat acaatgccac 1380
cgtttattcc caagcagcga atggcacaga aggacagccc caggccatag agttcaggac 1440
aaatgctatt caggtttttg acgtcaccgc tgtgaacatc agtgccacaa gcctgacct 1500
gatctggaag gtcagcgata acgagtcgtc atctaactat acctacaaga tacatgtggc 1560
gggggagaca gattcttcca atctcaacgt cagtgagcct cgcgctgtca tccccggact 1620
ccgctccagc accttctaca acatcacagt gtgtcctgtc ctaggtgaca tcgagggcac 1680
gccgggcttc ctccaagtgc acaccccccc tgttccagtt tctgacttcc gactgacagt 1740
ggtcagcacg acggagatcg gcttagcatg gagcagccat gatgcagaat catttcagat 1800
gcataatcaca caggaggggag ctggcaattc tcgggtagaa ataaccacca accaaagtat 1860
tatcattggt ggcttggtcc ctggaaccaa gtattgcttt gaaatagttc caaaaggacc 1920
aaatgggact gaaggggcat ctcgacagt ttgcaataga actgttccca gtgcagtgtt 1980
tgacatccac gtggtctacg tcaccaccac ggagatgtgg ctggactgga agagccctga 2040
cggtgcttcc gagtatgtct accatttagt catagagtcc aagcatggct ctaaccacac 2100
aagcacgtat gacaaagcga ttactctcca gggcctgatt ccgggcacct tatataacat 2160
caccatctct ccagaagtgg accacgtctg gggggacccc aactccactg cacagtacac 2220
acggcccagc aatgtgtcca acattgatgt aagtaccaac accacagcag caactttaag 2280
ttggcagaac tttgatgacg cctctcccac gtactcctac tgccttctta ttgagaaggc 2340
tggaatttcc agcaacgcaa cacaagtagt cacggacatt ggaattactg acgctacagt 2400
cactgaatta atacctggct catcatacac agtggagatc ttgacacaag taggggatgg 2460
gatcaagtca ctggaacctg gccggaagtc attctgtaca gatcctgcgt ccatggcctc 2520

```

```

cttcgactgc gaagtgggtcc ccaaagagcc agccctgggt ctcaaagtga cctgccctcc 2580
tgccgccaat gcaggctttg agctggaggt cagcagtggg gcctggaaca atgcgacca 2640
cctggagagc tgctcctctg agaatggcac tgagtataga acggaagtca cgtatttgaa 2700
tttttctacc tcgtacaaca tcagcatcac cactgtgtcc tgtggaaaga tggcagcccc 2760
caccgggaac acctgcacta ctggcatcac agatccccct cctccagatg gatccccctaa 2820
tattacatct gtcagtcaca attcagtaaa ggtcaagtcc agtggatttg aagccagcca 2880
cggacccatc aaagcctatg ctgtcattct caccaccggg gaagctgggt acccttctgc 2940
agatgtcctg aaatacacgt atgacgattt caaaaaggga gcctcagata cttatgtgac 3000
atacctcata agaacagaag aaaagggacg ttctcagagc ttgtctgaag ttttgaaata 3060
tgaaattgac gttgggaatg agtcaaccac acttgggttat tacaatggga agctggaacc 3120
tctgggctcc taccgggctt gtgtggctgg cttcaccaac attaccttc accctcaaaa 3180
caaggggctc attgatgggg ctgagagcta tgtgtccttc agtcgctact cagatgctgt 3240
ttccttgccc caggatccag gtgtcatctg tggagcgggt tttggctgta tctttgggtgc 3300
cctgggtatt gtgactgtgg gaggcttcat cttctggaga aagaagagga aagatgcaa 3360
gaataatgaa gtgtcctttt ctcaaattaa acctaaaaaa tctaagttaa tcagagtgg 3420
gaattttgag gcctacttca agaagcagca agctgactcc aactgtgggt tcgcagagga 3480
atacgaagat tctgaagctt tgggaattag tcaacctaaa tatgcagcag aactggctga 3540
gaatagagga aagaatcgct ataataatgt tctgccctat gatatttccc gtgtcaaact 3600
ttcgggtccag acccattcaa cggatgacta catcaatgcc aactacatgc ctggctacca 3660
ctccaagaaa gattttattg ccacacaagg acctttaccg aacactttga aagatttttg 3720
gcgtatgggt tgggagaaaa atgtatatgc catcattatg ttgactaaat gtgttgaaca 3780
gggaagaacc aaatgtgagg agtattggcc ctccaagcag gctcaggact atggagacat 3840
aactgtggca atgacatcag aaattgttct tccggaatgg accatcagag atttcacagt 3900
gaaaaatatc cagacaagtg agagtcaccc tctgagacag ttccatttca cctcctggcc 3960
agaccacggt gttcccagca ccactgacct gctcatcaac ttccggtacc tcgttcgtga 4020
ctacatgaag cagagtcctc ccgaatcgcc gattctgggt cattgcagtg ctggggctcg 4080
aaggacgggc actttcattg ccattgatcg tctcatctac cagatagaga atgagaacac 4140
cgtggatgtg tatgggattg tgtatgacct tcgaatgcat aggcctttaa tgggtgcagac 4200
agaggaccag tatgttttcc tcaatcagtg tgttttggat attgtcagat cccagaaaga 4260
ctcaaagta gatcttatct accagaacac aactgcaatg acaatctatg aaaaccttgc 4320
gcccgtgacc acatttggaag agaccaatgg ttacatcgcc taattccaaa ggaataacct 4380
ttctggagtg aaccagaccg tcgcaccac agcgaaggca catgccccga tgtcgacatg 4440
tttttatatg ttaatatct taattctttg ttctgttttg tgagaactaa ttttgagggc 4500
atgaagctgc atatgataga tgacaaattg gggctgtcgg gggctgtgga tgggtgggga 4560
gcaaatcatc tgcattcctg atgaccaatg ggatgaggtc actttttttt ttttccccct 4620
tgaggattgc ggaaaaccag gaaaagggat ctatgatttt tttttccaaa acaatttctt 4680
ttttaaaaag actattttat atgattcaca tgctaaagcc aggattgtgt tgggttgaat 4740
atatttttaag tatcagaggt ctatttttac ctactgtgtc ttggaatcta gccgatggaa 4800
aataccta atgtggatgat gattgcgcag ggaggggtac gtggcacctc ttccgaatgg 4860
gttttctatt tgaacatgtg ctttttctga attatgcttc cacaggcaaa actcagtaga 4920
gatctatatt tttgtactga atctcataat tggaatatac ggaatattta aacagtagct 4980
tagcatcaga ggtttgcttc ctcagtaaca tttctgttct catttgatca ggggaggcct 5040
ctttgccccg gccccgcttc cctgcccc gtgtgatttg tgctccattt tttcttccct 5100
tttccctccc agttttc 5117

```

<210> 38

<211> 1337

<212> PRT

<213> Homo sapiens

<400> 38

```

Met Lys Pro Ala Ala Arg Glu Ala Arg Leu Pro Pro Arg Ser Pro Gly
 1             5             10             15
Leu Arg Trp Ala Leu Pro Leu Leu Leu Leu Leu Arg Leu Gly Gln
                20             25             30
Ile Leu Cys Ala Gly Gly Thr Pro Ser Pro Ile Pro Asp Pro Ser Val

```


35	40	45
Ala Thr Val	Ala Thr Gly Glu Asn Gly Ile Thr Gln Ile Ser Ser Thr	
50	55	60
Ala Glu Ser Phe His Lys Gln Asn Gly Thr Gly Thr Pro Gln Val Glu		
65	70	75
Thr Asn Thr Ser Glu Asp Gly Glu Ser Ser Gly Ala Asn Asp Ser Leu		80
	85	90
Arg Thr Pro Glu Gln Gly Ser Asn Gly Thr Asp Gly Ala Ser Gln Lys		95
	100	105
Thr Pro Ser Ser Thr Gly Pro Ser Pro Val Phe Asp Ile Lys Ala Val		110
	115	120
Ser Ile Ser Pro Thr Asn Val Ile Leu Thr Trp Lys Ser Asn Asp Thr		125
	130	135
Ala Ala Ser Glu Tyr Lys Tyr Val Val Lys His Lys Met Glu Asn Glu		140
145	150	155
Lys Thr Ile Thr Val Val His Gln Pro Trp Cys Asn Ile Thr Gly Leu		160
	165	170
Arg Pro Ala Thr Ser Tyr Val Phe Ser Ile Thr Pro Gly Ile Gly Asn		175
	180	185
Glu Thr Trp Gly Asp Pro Arg Val Ile Lys Val Ile Thr Glu Pro Ile		190
	195	200
Pro Val Ser Asp Leu Arg Val Ala Leu Thr Gly Val Arg Lys Ala Ala		205
	210	215
Leu Ser Trp Ser Asn Gly Asn Gly Thr Ala Ser Cys Arg Val Leu Leu		220
225	230	235
Glu Ser Ile Gly Ser His Glu Glu Leu Thr Gln Asp Ser Arg Leu Gln		240
	245	250
Val Asn Ile Ser Asp Leu Lys Pro Gly Val Gln Tyr Asn Ile Asn Pro		255
	260	265
Tyr Leu Leu Gln Ser Asn Lys Thr Lys Gly Asp Pro Leu Gly Thr Glu		270
	275	280
Gly Gly Leu Asp Ala Ser Asn Thr Glu Arg Ser Arg Ala Gly Ser Pro		285
	290	295
Thr Ala Pro Val His Asp Glu Ser Leu Val Gly Pro Val Asp Pro Ser		300
305	310	315
Ser Gly Gln Gln Ser Arg Asp Thr Glu Val Leu Leu Val Gly Leu Glu		320
	325	330
Pro Gly Thr Arg Tyr Asn Ala Thr Val Tyr Ser Gln Ala Ala Asn Gly		335
	340	345
Thr Glu Gly Gln Pro Gln Ala Ile Glu Phe Arg Thr Asn Ala Ile Gln		350
	355	360
Val Phe Asp Val Thr Ala Val Asn Ile Ser Ala Thr Ser Leu Thr Leu		365
	370	375
Ile Trp Lys Val Ser Asp Asn Glu Ser Ser Ser Asn Tyr Thr Tyr Lys		380
385	390	395
Ile His Val Ala Gly Glu Thr Asp Ser Ser Asn Leu Asn Val Ser Glu		400
	405	410
Pro Arg Ala Val Ile Pro Gly Leu Arg Ser Ser Thr Phe Tyr Asn Ile		415
	420	425
Thr Val Cys Pro Val Leu Gly Asp Ile Glu Gly Thr Pro Gly Phe Leu		430
	435	440
Gln Val His Thr Pro Pro Val Ser Asp Phe Arg Val Thr Val		445
	450	455
Val Ser Thr Thr Glu Ile Gly Leu Ala Trp Ser Ser His Asp Ala Glu		460
465	470	475
Ser Phe Gln Met His Ile Thr Gln Glu Gly Ala Gly Asn Ser Arg Val		480
	485	490
Glu Ile Thr Thr Asn Gln Ser Ile Ile Ile Gly Gly Leu Phe Pro Gly		495

gcatgacgcg cggaggaggc agcgggagca gccgcgggag ccgggaccgg gtagccgcgc 60
gctgggggtg ggcgcgcgtc gctccgcccc gcgaagcccc tgcgcgctca gggacgcggc 120
ccccccgcgg cagccgcgct aggcctccgc gtgtggccgc ggccgcgcgc gccgctgcc 180

tgtctccggg	gaagcccg	gcgggcg	cggggacgag	gcggaccggc	tggcgaggga	240
ggaggcgaag	gagacggcag	gaggcgccga	cgacggtgcc	cgggctcggg	cgcacggcgg	300
ggcccgaattc	gcgcgtccgg	ggcacgttcc	agggcgcgcg	gggcatgaag	ccggcgggcg	360
gggaggcgcg	gctgcctccg	cgctcgcccc	ggctgcgctg	ggcgctgccg	ctgctgctgc	420
tgctgctgcg	cctggggccag	atcctgtgcg	cagggtggcac	ccctagtcca	attcctgacc	480
cttcagtagc	aactgttgcc	acaggggaaa	atggcataac	gcagatcagc	agtacagcag	540
aatcctttca	taaacagaat	ggaactggaa	cacctcaggt	ggaaacaaac	accagtgagg	600
atggtgaaag	ctctggagcc	aacgatagtt	taagaacacc	tgaacaagga	tctaattggga	660
ctgatggggc	atctcaaaaa	actcccagta	gcactggggc	cagtctgtg	tttgacatta	720
aagctgtttc	catcagttca	accaatgtga	tcttaacttg	gaaaagtaat	gacacagctg	780
cttctgagta	caagtatgta	gtaaagcata	agatggaaaa	tgagaagaca	attactgttg	840
tgcatcaacc	atggtgtaac	atcacaggct	tacgtccagc	gacttcatat	gtattctcca	900
tactccagg	aataggcaat	gagacttggg	gagatcccag	agtcataaaa	gtcatcacag	960
aaccgatccc	agttttctgat	ctccgtgttg	ccctcaecgg	tgtgagggaag	gctgctctct	1020
cctggagcaa	tggcaattggc	actgcctcct	gcccgggttct	tcttgaaagc	attggaagcc	1080
atgaggagtt	gactcaagac	tcaagacttc	aggtcaatat	ctcgggcctg	aagccagggg	1140
ttcaatacaa	catcaaccgg	tatcttctac	aatcaaataa	gacaaaggga	gaccccttgg	1200
gcacagaagg	tggcttggat	gccagcaata	cagagagaag	ccgggcaggg	agccccaccg	1260
ccctgtgca	tgatgagtcc	ctcgtgggac	ctgtggaccc	atcctccggc	cagcagttcc	1320
gagacacgga	agtctgtctt	gtcgggttag	agcctggcac	ccgatacaat	gccaccgttt	1380
attccaagc	agcgaatggc	acagaaggac	agccccaggc	catagagttc	aggacaaatg	1440
ctattcaggt	ttttgacgtc	accgctgtga	acatcagtg	cacaagcctg	accctgatct	1500
ggaaagtcag	cgataacgag	tcgtcatcta	actataccta	caagatacat	gtggcggggg	1560
agacagattc	ttccaatctc	aacgtcagtg	agcctcgcg	tgtcatcccc	ggactccgct	1620
ccagcacctt	ctacaacatc	acagtgtgtc	ctgtcctagg	tgacatcgag	ggcacgccc	1680
gcttctccca	agtgcacacc	ccccctgttc	cagtttctga	cttccgagtg	acagtgggtca	1740
gcacgacgga	gatcggttta	gcatggagca	gccatgatgc	agaatcattt	cagatgcata	1800
tcacacagga	gggagctggc	aattctcggg	tagaaataac	caccaaccaa	agtattatca	1860
ttggtggcct	gttccttggg	accaagtatt	gctttgaaat	agttccaaaa	ggaccaaattg	1920
ggactgaagg	ggcatctcgg	acagtgttga	atagaactgt	tcccagtgca	gtgttttgaca	1980
tccacgtggt	ctacgtcacc	accacggaga	tgtggctgga	ctggaagagc	cctgacggtg	2040
cttccgagta	tgtctaccat	ttagtcatag	agtccaagca	tggtcttaac	cacacaagca	2100
cgtatgacaa	agcgattact	ctccaggggc	tgattccggg	cacettatat	aacatcacca	2160
tctctccaga	agtggaccac	gtctgggggg	accccaactc	cactgcacag	tacacacggc	2220
ccagcaatgt	gtccaacatt	gatgtaagta	ccaacaccac	agcagcaact	ttaagttggc	2280
agaactttga	tgacgcctct	cccacgtact	cctactgcct	tcttattgag	aaggctggaa	2340
attccagcaa	cgcaacacaa	gtagtacagg	acattggaat	tactgacgct	acagtcacga	2400
aattaatacc	tggctcatca	tacacagtgg	agatctttgc	acaagtaggg	gatgggatca	2460
agtcactgga	acctggccgg	aagtcatctt	gtacagatcc	tgcgtccatg	gcctccttcg	2520
actgcgaagt	gggtcccaaa	gagccagccc	tggttctcaa	atggacctgc	cctcctggcg	2580
ccaatgcagg	ctttgagctg	gaggtcagca	gtggagcctg	gaacaatgcg	accacactgg	2640
agagctgctc	ctctgagaat	ggcactgagt	atagaacgga	agtcacgtat	ttgaattttt	2700
ctacctcgta	caacatcagc	atcaccactg	tgtcctgtgg	aaagatggca	gccccacccc	2760
ggaacacctg	cactactggc	atcacagatc	cccctcctcc	agatggatcc	cctaataatta	2820
catctgtcag	tcacaattca	gtaaagggtca	agttcagtg	atgtgaagcc	agccacggac	2880
ccatcaaagc	ctatgctgtc	attctcacca	ccggggaagc	tggtcaccct	tctgcagatg	2940
tcttgaaata	cacgtatgac	gatttcaaaa	agggagcctc	agatacttat	gtgacatacc	3000
tcataagaac	agaagaaaag	ggacgttctc	agagcttgtc	tgaagttttg	aaatatgaaa	3060
ttgacgttgg	gaatgagtca	accacacttg	gttattttaca	atgggaagct	ggaacctctg	3120
ggctcctacc	ggcttgtgtg	gctggcttca	ccaacattac	cttccaccct	caaaacaagg	3180
ggctcattga	tggggctgag	agctatgtgt	ccttcagtcg	ctactcagat	gctgtttcct	3240
tgccccagga	tccaggtgtc	atctgtggag	cggtttttgg	ctgtatcttt	ggtgccctgg	3300
ttattgtgac	tgtgggaggc	ttcatctctc	ggagaaaaga	gaggaaaagat	gcaaagaata	3360
atgaagtgtc	cttttctcaa	attaaacctc	aaaaatctaa	gttaatcaga	gtggagaatt	3420
ttgaggccta	cttcaagaag	cagcaagctg	actccaactg	tgggttcgca	gaggaatacg	3480
aagatctgaa	gcttggttga	attagtcaac	ctaaatatgc	agcagaactg	gctgagaata	3540
gaggaaagaa	tcgctataat	aatgttctgc	cctatgatat	ttcccggtgc	aaactttcgg	3600
tccagaccca	ttcaacggat	gactacatca	atgccaaacta	catgcctggc	taccactcca	3660

```

agaaagattt tattgccaca caaggacctt taccgaacac tttgaaagat ttttggcgta 3720
tggtttggga gaaaaatgta tatgccatca ttatgttgac taaatgtggt gaacagggaa 3780
gaaccaaagt tgaggagtat tggccctcca agcaggctca ggactatgga gacataactg 3840
tggcaatgac atcagaaatt gttcttcctg aatggaccat cagagatttc acagtgaaaa 3900
atatccagac aagtgagagt caccctctga gacagttcca tttcacctcc tggccagacc 3960
acgggtgttc cgacaccact gacctgctca tcaacttcct gtacctcgtt cgtgactaca 4020
tgaagcagag tcctcccgaa tcgccgattc tgggtgcattg cagtgtctggg gtcggaagga 4080
cgggcacttt cattgccatt gatcgtctca tctaccagat agagaatgag aacaccgtgg 4140
atgtgtatgg gattgtgtat gaccttcgaa tgcataaggcc tttaatggtg cagacagagg 4200
accagtatgt tttcctcaat cagtgtgttt tggatattgt cagatcccag aaagactcaa 4260
aagtagatct tatctaccag aacacaactg caatgacaat ctatgaaaac cttgcgcccg 4320
tgaccacatt tggaaagacc aatgggttaca tcgcctaatt ccaaaggaat aacctttctg 4380
gagtgaacca gaccgtcgca cccacagcga aggcacatgc ccgatgtcga catgttttat 4440
atgctaatat cttaattctt tgttctgttt tgtgagaact aattttgagg gcatgaagct 4500
gcatatcata gatgacaaat tggggctgtc gggggctgtg gatgggtggg gagcaaatca 4560
tctgcattcc tgatgacaa tgggatgagg tcactttttt tttttttccc ccttcgaagg 4620
attgtggaaa accaggaaaaa gggagctatg attttttttt ccaaaacaat ttctttttta 4680
aaaaagacta tttatatgat tcacatgcta aagccaggat tgtgttggtg tgaatatatt 4740
ttaagtatca gaggtc 4756

```

<210> 40

<211> 1337

<212> PRT

<213> Homo sapiens

<400> 40

```

Met Lys Pro Ala Ala Arg Glu Ala Arg Leu Pro Pro Arg Ser Pro Gly
1          5          10          15
Leu Arg Trp Ala Leu Pro Leu Leu Leu Leu Leu Leu Arg Leu Gly Gln
20          25          30
Ile Leu Cys Ala Gly Gly Thr Pro Ser Pro Ile Pro Asp Pro Ser Val
35          40          45
Ala Thr Val Ala Thr Gly Glu Asn Gly Ile Thr Gln Ile Ser Ser Thr
50          55          60
Ala Glu Ser Phe His Lys Gln Asn Gly Thr Gly Thr Pro Gln Val Glu
65          70          75          80
Thr Asn Thr Ser Glu Asp Gly Glu Ser Ser Gly Ala Asn Asp Ser Leu
85          90          95
Arg Thr Pro Glu Gln Gly Ser Asn Gly Thr Asp Gly Ala Ser Gln Lys
100         105         110
Thr Pro Ser Ser Thr Gly Pro Ser Pro Val Phe Asp Ile Lys Ala Val
115         120         125
Ser Ile Ser Pro Thr Asn Val Ile Leu Thr Trp Lys Ser Asn Asp Thr
130         135         140
Ala Ala Ser Glu Tyr Lys Tyr Val Val Lys His Lys Met Glu Asn Glu
145         150         155         160
Lys Thr Ile Thr Val Val His Gln Pro Trp Cys Asn Ile Thr Gly Leu
165         170         175
Arg Pro Ala Thr Ser Tyr Val Phe Ser Ile Thr Pro Gly Ile Gly Asn
180         185         190
Glu Thr Trp Gly Asp Pro Arg Val Ile Lys Val Ile Thr Glu Pro Ile
195         200         205
Pro Val Ser Asp Leu Arg Val Ala Leu Thr Gly Val Arg Lys Ala Ala
210         215         220
Leu Ser Trp Ser Asn Gly Asn Gly Thr Ala Ser Cys Arg Val Leu Leu
225         230         235         240
Glu Ser Ile Gly Ser His Glu Glu Leu Thr Gln Asp Ser Arg Leu Gln
245         250         255

```

Val	Asn	Ile	Ser	Gly	Leu	Lys	Pro	Gly	Val	Gln	Tyr	Asn	Ile	Asn	Pro		
			260					265					270				
Tyr	Leu	Leu	Gln	Ser	Asn	Lys	Thr	Lys	Gly	Asp	Pro	Leu	Gly	Thr	Glu		
		275					280					285					
Gly	Gly	Leu	Asp	Ala	Ser	Asn	Thr	Glu	Arg	Ser	Arg	Ala	Gly	Ser	Pro		
	290					295				300							
Thr	Ala	Pro	Val	His	Asp	Glu	Ser	Leu	Val	Gly	Pro	Val	Asp	Pro	Ser		
305				310						315					320		
Ser	Gly	Gln	Gln	Ser	Arg	Asp	Thr	Glu	Val	Leu	Leu	Val	Gly	Leu	Glu		
			325						330					335			
Pro	Gly	Thr	Arg	Tyr	Asn	Ala	Thr	Val	Tyr	Ser	Gln	Ala	Ala	Asn	Gly		
		340						345				350					
Thr	Glu	Gly	Gln	Pro	Gln	Ala	Ile	Glu	Phe	Arg	Thr	Asn	Ala	Ile	Gln		
		355					360					365					
Val	Phe	Asp	Val	Thr	Ala	Val	Asn	Ile	Ser	Ala	Thr	Ser	Leu	Thr	Leu		
	370					375					380						
Ile	Trp	Lys	Val	Ser	Asp	Asn	Glu	Ser	Ser	Ser	Asn	Tyr	Thr	Tyr	Lys		
385				390						395					400		
Ile	His	Val	Ala	Gly	Glu	Thr	Asp	Ser	Ser	Asn	Leu	Asn	Val	Ser	Glu		
			405						410					415			
Pro	Arg	Ala	Val	Ile	Pro	Gly	Leu	Arg	Ser	Ser	Thr	Phe	Tyr	Asn	Ile		
		420						425				430					
Thr	Val	Cys	Pro	Val	Leu	Gly	Asp	Ile	Glu	Gly	Thr	Pro	Gly	Phe	Leu		
		435					440					445					
Gln	Val	His	Thr	Pro	Pro	Val	Pro	Val	Ser	Asp	Phe	Arg	Val	Thr	Val		
	450					455					460						
Val	Ser	Thr	Thr	Glu	Ile	Gly	Leu	Ala	Trp	Ser	Ser	His	Asp	Ala	Glu		
465				470						475					480		
Ser	Phe	Gln	Met	His	Ile	Thr	Gln	Glu	Gly	Ala	Gly	Asn	Ser	Arg	Val		
			485						490					495			
Glu	Ile	Thr	Thr	Asn	Gln	Ser	Ile	Ile	Ile	Gly	Gly	Leu	Phe	Pro	Gly		
			500					505					510				
Thr	Lys	Tyr	Cys	Phe	Glu	Ile	Val	Pro	Lys	Gly	Pro	Asn	Gly	Thr	Glu		
		515					520					525					
Gly	Ala	Ser	Arg	Thr	Val	Cys	Asn	Arg	Thr	Val	Pro	Ser	Ala	Val	Phe		
	530					535					540						
Asp	Ile	His	Val	Val	Tyr	Val	Thr	Thr	Thr	Glu	Met	Trp	Leu	Asp	Trp		
545				550						555					560		
Lys	Ser	Pro	Asp	Gly	Ala	Ser	Glu	Tyr	Val	Tyr	His	Leu	Val	Ile	Glu		
			565					570						575			
Ser	Lys	His	Gly	Ser	Asn	His	Thr	Ser	Thr	Tyr	Asp	Lys	Ala	Ile	Thr		
			580				585					590					
Leu	Gln	Gly	Leu	Ile	Pro	Gly	Thr	Leu	Tyr	Asn	Ile	Thr	Ile	Ser	Pro		
		595					600					605					
Glu	Val	Asp	His	Val	Trp	Gly	Asp	Pro	Asn	Ser	Thr	Ala	Gln	Tyr	Thr		
	610					615					620						
Arg	Pro	Ser	Asn	Val	Ser	Asn	Ile	Asp	Val	Ser	Thr	Asn	Thr	Thr	Ala		
625				630						635					640		
Ala	Thr	Leu	Ser	Trp	Gln	Asn	Phe	Asp	Asp	Ala	Ser	Pro	Thr	Tyr	Ser		
			645					650						655			
Tyr	Cys	Leu	Leu	Ile	Glu	Lys	Ala	Gly	Asn	Ser	Ser	Asn	Ala	Thr	Gln		
			660					665					670				
Val	Val	Thr	Asp	Ile	Gly	Ile	Thr	Asp	Ala	Thr	Val	Thr	Glu	Leu	Ile		
		675					680					685					
Pro	Gly	Ser	Ser	Tyr	Thr	Val	Glu	Ile	Phe	Ala	Gln	Val	Gly	Asp	Gly		
	690					695					700						
Ile	Lys	Ser	Leu	Glu	Pro	Gly	Arg	Lys	Ser	Phe	Cys	Thr	Asp	Pro	Ala		
705					710					715					720		

Ser Met Ala Ser Phe Asp Cys Glu Val Val Pro Lys Glu Pro Ala Leu
 725 730 735
 Val Leu Lys Trp Thr Cys Pro Pro Gly Ala Asn Ala Gly Phe Glu Leu
 740 745 750
 Glu Val Ser Ser Gly Ala Trp Asn Asn Ala Thr His Leu Glu Ser Cys
 755 760 765
 Ser Ser Glu Asn Gly Thr Glu Tyr Arg Thr Glu Val Thr Tyr Leu Asn
 770 775 780
 Phe Ser Thr Ser Tyr Asn Ile Ser Ile Thr Thr Val Ser Cys Gly Lys
 785 790 795 800
 Met Ala Ala Pro Thr Arg Asn Thr Cys Thr Thr Gly Ile Thr Asp Pro
 805 810 815
 Pro Pro Pro Asp Gly Ser Pro Asn Ile Thr Ser Val Ser His Asn Ser
 820 825 830
 Val Lys Val Lys Phe Ser Gly Phe Glu Ala Ser His Gly Pro Ile Lys
 835 840 845
 Ala Tyr Ala Val Ile Leu Thr Thr Gly Glu Ala Gly His Pro Ser Ala
 850 855 860
 Asp Val Leu Lys Tyr Thr Tyr Asp Asp Phe Lys Lys Gly Ala Ser Asp
 865 870 875 880
 Thr Tyr Val Thr Tyr Leu Ile Arg Thr Glu Glu Lys Gly Arg Ser Gln
 885 890 895
 Ser Leu Ser Glu Val Leu Lys Tyr Glu Ile Asp Val Gly Asn Glu Ser
 900 905 910
 Thr Thr Leu Gly Tyr Leu Gln Trp Glu Ala Gly Thr Ser Gly Leu Leu
 915 920 925
 Pro Ala Cys Val Ala Gly Phe Thr Asn Ile Thr Phe His Pro Gln Asn
 930 935 940
 Lys Gly Leu Ile Asp Gly Ala Glu Ser Tyr Val Ser Phe Ser Arg Tyr
 945 950 955 960
 Ser Asp Ala Val Ser Leu Pro Gln Asp Pro Gly Val Ile Cys Gly Ala
 965 970 975
 Val Phe Gly Cys Ile Phe Gly Ala Leu Val Ile Val Thr Val Gly Gly
 980 985 990
 Phe Ile Phe Trp Arg Lys Lys Arg Lys Asp Ala Lys Asn Asn Glu Val
 995 1000 1005
 Ser Phe Ser Gln Ile Lys Pro Lys Lys Ser Lys Leu Ile Arg Val Glu
 1010 1015 1020
 Asn Phe Glu Ala Tyr Phe Lys Lys Gln Gln Ala Asp Ser Asn Cys Gly
 1025 1030 1035 1040
 Phe Ala Glu Glu Tyr Glu Asp Leu Lys Leu Val Gly Ile Ser Gln Pro
 1045 1050 1055
 Lys Tyr Ala Ala Glu Leu Ala Glu Asn Arg Gly Lys Asn Arg Tyr Asn
 1060 1065 1070
 Asn Val Leu Pro Tyr Asp Ile Ser Arg Val Lys Leu Ser Val Gln Thr
 1075 1080 1085
 His Ser Thr Asp Asp Tyr Ile Asn Ala Asn Tyr Met Pro Gly Tyr His
 1090 1095 1100
 Ser Lys Lys Asp Phe Ile Ala Thr Gln Gly Pro Leu Pro Asn Thr Leu
 1105 1110 1115 1120
 Lys Asp Phe Trp Arg Met Val Trp Glu Lys Asn Val Tyr Ala Ile Ile
 1125 1130 1135
 Met Leu Thr Lys Cys Val Glu Gln Gly Arg Thr Lys Cys Glu Glu Tyr
 1140 1145 1150
 Trp Pro Ser Lys Gln Ala Gln Asp Tyr Gly Asp Ile Thr Val Ala Met
 1155 1160 1165
 Thr Ser Glu Ile Val Leu Pro Glu Trp Thr Ile Arg Asp Phe Thr Val
 1170 1175 1180

Lys Asn Ile Gln Thr Ser Glu Ser His Pro Leu Arg Gln Phe His Phe
 1185 1190 1195 1200
 Thr Ser Trp Pro Asp His Gly Val Pro Asp Thr Thr Asp Leu Leu Ile
 1205 1210 1215
 Asn Phe Arg Tyr Leu Val Arg Asp Tyr Met Lys Gln Ser Pro Pro Glu
 1220 1225 1230
 Ser Pro Ile Leu Val His Cys Ser Ala Gly Val Gly Arg Thr Gly Thr
 1235 1240 1245
 Phe Ile Ala Ile Asp Arg Leu Ile Tyr Gln Ile Glu Asn Glu Asn Thr
 1250 1255 1260
 Val Asp Val Tyr Gly Ile Val Tyr Asp Leu Arg Met His Arg Pro Leu
 1265 1270 1275 1280
 Met Val Gln Thr Glu Asp Gln Tyr Val Phe Leu Asn Gln Cys Val Leu
 1285 1290 1295
 Asp Ile Val Arg Ser Gln Lys Asp Ser Lys Val Asp Leu Ile Tyr Gln
 1300 1305 1310
 Asn Thr Thr Ala Met Thr Ile Tyr Glu Asn Leu Ala Pro Val Thr Thr
 1315 1320 1325
 Phe Gly Lys Thr Asn Gly Tyr Ile Ala
 1330 1335

<210> 41
 <211> 122
 <212> PRT
 <213> Homo sapiens

<400> 41
 Trp Arg Met Val Trp Glu Gln Asn Val Tyr Ala Ile Ile Met Leu Thr
 1 5 10 15
 Lys Cys Val Glu Gln Gly Arg Thr Lys Cys Glu Glu Tyr Trp Pro Ser
 20 25 30
 Lys Gln Ala Gln Asp Tyr Gly Asp Ile Thr Val Ala Met Thr Ser Glu
 35 40 45
 Ile Val Leu Pro Glu Trp Thr Ile Arg Asp Phe Thr Val Lys Asn Ile
 50 55 60
 Gln Thr Ser Glu Ser His Pro Leu Arg Gln Phe His Phe Thr Ser Trp
 65 70 75 80
 Pro Asp His Gly Val Pro Asp Thr Thr Asp Leu Leu Ile Asn Phe Arg
 85 90 95
 Tyr Leu Val Arg Asp Tyr Met Lys Gln Ser Pro Pro Glu Ser Glu Ile
 100 105 110
 Leu Val His Cys Ser Ala Gly Ile Gly Arg
 115 120

<210> 42
 <211> 2543
 <212> DNA
 <213> Homo sapiens

<400> 42
 cggccccagg cctggagggg ggtctgtgcg cggccggctg gctctgcccc gcgtccggtc 60
 ccgagcgggc ctccctcggg ccagcccgat gtgaccgagc ccagcgggagc ctgagcaagg 120
 agcgggtccg tcgcggagcc ggagggcggg aggaacatga catcgcgag atggtttcac 180
 ccaaataatca ctggtgtgga ggcagaaaac ctactgttga caagaggagt tgatggcagt 240
 tttttggcaa ggcctagtaa aagtaacctt ggagacttca cactttccgt tagaagaaat 300
 ggagctgtca cccacatcaa gattcagaac actggtgatt actatgacct gtatggaggg 360


```

gagaaatttg ccactttggc tgagttgggc cagtattaca tggaacatca cgggcaatta 420
aaagagaaga atggagatgt cattgagctt aaatatcctc tgaactgtgc agatcctacc 480
tctgaaaggt ggtttcatgg acatctctct gggaaagaag cagagaaatt attaactgaa 540
aaagggaaac atggtagttt tcttgtacga gagagccaga gccaccctgg agattttgtt 600
ctttctgtgc gcaactggtga tgacaaaggg gagagcaatg acggcaagtc taaagtgacc 660
catgttatga ttcgctgtca ggaactgaaa tacgacgttg gtggaggaga acggtttgat 720
tctttgacag atcttgtgga acattataag aagaatccta tgggtgaaac attgggtaca 780
gtactacaac tcaagcagcc ccttaacacg actcgtataa atgctgctga aatagaaagc 840
agagttcgag aactaagcaa attagctgag accacagata aagtcaaaca aggcttttgg 900
gaagaatttg agacactaca acaacaggag tgcaaacctc tctacagcgc aaaagagggg 960
caaaggcaag aaaacaaaaa caaaaataga tataaaaaa tcttgcctt tgatcatacc 1020
agggttgtcc tacacgatgg tgatcccaat gagcctgttt cagattacat caatgcaaatt 1080
atcatcatgc ctgaatttga aaccaagtgc aacaattcaa agcccaaaaa gagttacatt 1140
gccacacaag gctgcctgca aaacacgggt aatgactttt ggcggtgggt gttccaagaa 1200
aactcccag tgattgtcat gacaacgaaa gaagtggaga gaggaaagag taaatgtgtc 1260
aaatactggc ctgatgagta tgctctaaaa gaatatggcg tcatgcgtgt taggaacgtc 1320
aaagaaagcg ccgctcatga ctatacgcta agagaactta aactttcaaa ggttggacaa 1380
gggaatacgg agagaacgggt ctggcaatac cactttcgga cctggccgga ccacggcgtg 1440
cccagcgacc ctgggggctg gctggacttc ctggaggagg tgcaccataa gcaggagagc 1500
atcatggatg cagggccggt cgtggtgcac tgcagtgtg gaattggccg gacagggacg 1560
ttcattgtga ttgatattct tattgacatc atcagagaga aaggtgttga ctgcgatatt 1620
gacgttccca aaaccatcca gatggtgcgg tctcagaggt cagggatgggt ccagacagaa 1680
gcacagtacc gatttatcta tatggcggtc cagcattata ttgaaacact acagcgagg 1740
attgaagaag agcagaaaag gaagaggaaa gggcacgaat atacaaatat taagtatcct 1800
ctagcggacc agacgagtgg agatcagagc cctctccgc cttgtactcc aacgccaccc 1860
tgtgcagaaa tgagagaaga cagtgtctga gtctatgaaa acgtgggcct gatgcaacag 1920
cagaaaagtt tcagatgaga aaacctgcca aaacttcagc acagaaatag atgtggactt 1980
tcaccctctc cctaaaaaga tcaagaacag acgcaagaaa gtttatgtga agacagaatt 2040
tggatttga aggttgcaa tgtggttgac taccttttga taagcaaaat ttgaaacat 2100
ttaagacca ctgtatttta actcaacaat acctgcttcc caattactca tttcctcaga 2160
taagaagaaa tcatctctac aatgtagaca acattatatt ttatagaatt tgtttgaaat 2220
tgaggaagca gttaaattgt gcgctgtatt ttgcagatta tggggattca aattctagta 2280
ataggctttt ttatttttat ttttataccc ttaaccagtt taattttttt tttcctcatt 2340
gttggggatg atgagaagaa atgatttggg aaaattaagt aacaacgacc tagaaaagtg 2400
agaacaatct catttaccat catgtatcca gtatgggata attcattttg atggcttcta 2460
tttttggcca aatgagaata agccagtgcc tgagactgtc agaagttgac ctttgcactg 2520
gcattaaaga gtcatagaaa aaa
2543

```

<210> 43

<211> 593

<212> PRT

<213> Homo sapiens

<400> 43

```

Met Thr Ser Arg Arg Trp Phe His Pro Asn Ile Thr Gly Val Glu Ala
1      5      10      15
Glu Asn Leu Leu Leu Thr Arg Gly Val Asp Gly Ser Phe Leu Ala Arg
20     25     30
Pro Ser Lys Ser Asn Pro Gly Asp Phe Thr Leu Ser Val Arg Arg Asn
35     40     45
Gly Ala Val Thr His Ile Lys Ile Gln Asn Thr Gly Asp Tyr Tyr Asp
50     55     60
Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu Ala Glu Leu Val Gln Tyr
65     70     75     80
Tyr Met Glu His His Gly Gln Leu Lys Glu Lys Asn Gly Asp Val Ile
85     90     95
Glu Leu Lys Tyr Pro Leu Asn Cys Ala Asp Pro Thr Ser Glu Arg Trp
100    105    110

```

Phe	His	Gly	His	Leu	Ser	Gly	Lys	Glu	Ala	Glu	Lys	Leu	Leu	Thr	Glu		
		115					120					125					
Lys	Gly	Lys	His	Gly	Ser	Phe	Leu	Val	Arg	Glu	Ser	Gln	Ser	His	Pro		
		130				135					140						
Gly	Asp	Phe	Val	Leu	Ser	Val	Arg	Thr	Gly	Asp	Asp	Lys	Gly	Glu	Ser		
145					150					155					160		
Asn	Asp	Gly	Lys	Ser	Lys	Val	Thr	His	Val	Met	Ile	Arg	Cys	Gln	Glu		
				165					170					175			
Leu	Lys	Tyr	Asp	Val	Gly	Gly	Gly	Glu	Arg	Phe	Asp	Ser	Leu	Thr	Asp		
		180						185					190				
Leu	Val	Glu	His	Tyr	Lys	Lys	Asn	Pro	Met	Val	Glu	Thr	Leu	Gly	Thr		
		195					200					205					
Val	Leu	Gln	Leu	Lys	Gln	Pro	Leu	Asn	Thr	Thr	Arg	Ile	Asn	Ala	Ala		
		210				215					220						
Glu	Ile	Glu	Ser	Arg	Val	Arg	Glu	Leu	Ser	Lys	Leu	Ala	Glu	Thr	Thr		
225					230					235					240		
Asp	Lys	Val	Lys	Gln	Gly	Phe	Trp	Glu	Glu	Phe	Glu	Thr	Leu	Gln	Gln		
				245					250					255			
Gln	Glu	Cys	Lys	Leu	Leu	Tyr	Ser	Arg	Lys	Glu	Gly	Gln	Arg	Gln	Glu		
			260					265					270				
Asn	Lys	Asn	Lys	Asn	Arg	Tyr	Lys	Asn	Ile	Leu	Pro	Phe	Asp	His	Thr		
		275				280						285					
Arg	Val	Val	Leu	His	Asp	Gly	Asp	Pro	Asn	Glu	Pro	Val	Ser	Asp	Tyr		
		290				295					300						
Ile	Asn	Ala	Asn	Ile	Ile	Met	Pro	Glu	Phe	Glu	Thr	Lys	Cys	Asn	Asn		
305				310						315					320		
Ser	Lys	Pro	Lys	Lys	Ser	Tyr	Ile	Ala	Thr	Gln	Gly	Cys	Leu	Gln	Asn		
			325						330					335			
Thr	Val	Asn	Asp	Phe	Trp	Arg	Met	Val	Phe	Gln	Glu	Asn	Ser	Arg	Val		
		340					345						350				
Ile	Val	Met	Thr	Thr	Lys	Glu	Val	Glu	Arg	Gly	Lys	Ser	Lys	Cys	Val		
		355				360						365					
Lys	Tyr	Trp	Pro	Asp	Glu	Tyr	Ala	Leu	Lys	Glu	Tyr	Gly	Val	Met	Arg		
		370				375					380						
Val	Arg	Asn	Val	Lys	Glu	Ser	Ala	Ala	His	Asp	Tyr	Thr	Leu	Arg	Glu		
385				390						395					400		
Leu	Lys	Leu	Ser	Lys	Val	Gly	Gln	Gly	Asn	Thr	Glu	Arg	Thr	Val	Trp		
				405					410					415			
Gln	Tyr	His	Phe	Arg	Thr	Trp	Pro	Asp	His	Gly	Val	Pro	Ser	Asp	Pro		
			420					425					430				
Gly	Gly	Val	Leu	Asp	Phe	Leu	Glu	Glu	Val	His	His	Lys	Gln	Glu	Ser		
		435					440					445					
Ile	Met	Asp	Ala	Gly	Pro	Val	Val	Val	His	Cys	Ser	Ala	Gly	Ile	Gly		
		450				455					460						
Arg	Thr	Gly	Thr	Phe	Ile	Val	Ile	Asp	Ile	Leu	Ile	Asp	Ile	Ile	Arg		
465				470						475					480		
Glu	Lys	Gly	Val	Asp	Cys	Asp	Ile	Asp	Val	Pro	Lys	Thr	Ile	Gln	Met		
				485				490						495			
Val	Arg	Ser	Gln	Arg	Ser	Gly	Met	Val	Gln	Thr	Glu	Ala	Gln	Tyr	Arg		
		500					505						510				
Phe	Ile	Tyr	Met	Ala	Val	Gln	His	Tyr	Ile	Glu	Thr	Leu	Gln	Arg	Arg		
		515				520						525					
Ile	Glu	Glu	Glu	Gln	Lys	Arg	Lys	Arg	Lys	Gly	His	Glu	Tyr	Thr	Asn		
		530				535					540						
Ile	Lys	Tyr	Pro	Leu	Ala	Asp	Gln	Thr	Ser	Gly	Asp	Gln	Ser	Pro	Leu		
545				550						555					560		
Pro	Pro	Cys	Thr	Pro	Thr	Pro	Pro	Cys	Ala	Glu	Met	Arg	Glu	Asp	Ser		
				565					570					575			

Ala Arg Val Tyr Glu Asn Val Gly Leu Met Gln Gln Gln Lys Ser Phe
580 585 590

Arg

```
<210> 44
<211> 2276
<212> DNA
<213> Homo sapiens
```

<400> 44						
ctgccccgcg	tccgggtccc	agcggggcctc	cctcggggcca	gcccgatgtg	accgagccca	60
gcggagcctg	agcaaggagc	gggtccgtcg	cggagccgga	gggcgggagg	aacatgacat	120
gcgggagatg	gtttcaccca	aatatcactg	gtgtggaggc	agaaaaccta	ctgttgacaa	180
gaggagtgtg	tggcagtttt	ttggcaaggc	ctagtaaaag	taaccttgga	gacttcacac	240
tttccgttag	aagaaatgga	gctgtcacc	acatcaagat	tcagaacact	ggtgattact	300
atgacctgta	tggaggggag	aaatttgcca	ctttggctga	gttgggtccag	tattacatgg	360
aacatcacgg	gcaattaaaa	gagaagaatg	gagatgtcat	tgagcttaaa	tatcctctga	420
actgtgcaga	tcctacctct	gaaaggtggt	ttcatggaca	tctctctggg	aaagaagcag	480
agaaattatt	aactgaaaaa	ggaaaacatg	gtagttttct	tgtacgagag	agccagagcc	540
accctggaga	ttttgttctt	tctgtgcgca	ctgggtgatga	caaaggggag	agcaatgacg	600
gcaagtctaa	agtgacccat	gttatgattc	gctgtcagga	actgaaatac	gacgttgggtg	660
gaggagaacg	gtttgattct	ttgacagatc	ttgtggaaca	ttataagaag	aatcctatgg	720
tggaaacatt	gggtacagta	ctacaactca	agcagccctt	taacacgact	cgtataaatg	780
ctgctgaaat	agaaagcaga	gttcgagAAC	taagcaaatt	agctgagacc	acagataaag	840
tcaaacaagg	cttttgggaa	gaatttgaga	cactacaaca	acaggagtgc	aaacttctct	900
acagccgaaa	agaggggtcaa	aggcaagaaa	acaaaaacaa	aaatagatat	aaaaacatcc	960
tgccttttga	tcataccagg	tttgtcctac	acgatgggtga	tcccaatgag	cctgttttcag	1020
attacattcaa	tgcaaaatate	atctatcgctg	aaattggaac	caagtgcAAC	aattcaaagc	1080
ccaaaaagag	ttacattgcc	acacaaggct	gcctgcaaaa	cacggtgaat	gacttttggc	1140
ggatgggtgt	ccaagaaaac	tcccagagtga	ttgtcatgac	aacgaaagaa	gtggagagag	1200
gaaagagtaa	atgtgtcaaa	tactggcctg	atgagtatgc	tctaaaagaa	tatggcgctca	1260
tgcgtgttag	gaacgtcaaa	gaaagcgccg	ctcatgacta	tacgctaaga	gaacttaaac	1320
tttcaaaggt	tggacaagggt	aatacggaga	gaacgggtctg	gcaataccac	tttcggacct	1380
ggccggacca	cggcgtgccc	agcgaccctg	ggggcgtgct	ggacttctctg	gaggaggtgc	1440
accataagca	ggagagcatc	atggatgcag	ggccgggtcgt	ggtgcactgc	agtgtcggaa	1500
ttggccggac	agggacgttc	attgtgattg	atattcttat	tgacatcatc	agagagaaag	1560
gtgttgactg	cgatattgac	gttcccaaaa	ccatccagat	ggtgcggtct	cagagggtcag	1620
ggatgggtcca	gacagaagca	cagtaccgat	ttatctatat	ggcgggtccag	catttatattg	1680
aaacactaca	gcgcaggatt	gaagaagagc	agaaaagcaa	gaggaaaggg	cacgaatata	1740
caaatattaa	gtattctcta	gcggaccaga	cgagtggaga	tcagagccct	ctccgcctt	1800
gtactccaac	gccaccctgt	gcagaaatga	gagaagacag	tgctagagtc	tatgaaaacg	1860
tgggcctgat	gcaacagcag	aaaagtttca	gatgagaaaa	cctgccaaaa	cttcagcaca	1920
gaaatagatg	tggactttca	ccctctccct	aaaaagatca	agaacagacg	caagaaagtt	1980
tatgtgaaga	cagaattttg	atttggcaagg	cttgcaatgt	ggttgactac	cttttgataa	2040
gcaaaatttg	aaaccattta	aagaccactg	tatttttaact	caacaatacc	tgcttcccaa	2100
ttactcattt	cctcagataa	gaagaaatca	tctctacaat	ctgagacaaca	ttatatttta	2160
tagaatttgt	ttgaaattga	ggaaagcagtt	aaattgtgcg	gtgtattttg	cagatttatgg	2220
ggattcaaat	tctagtaata	ggctttttta	tttttatttt	tataccctta	accagg	2276

```
<210> 45
<211> 593
<212> PRT
<213> Homo sapiens
```

<400> 45
Met Thr Ser Arg Arg Trp Phe His Pro Asn Ile Thr Gly Val Glu Ala

1	5	10	15
Glu Asn Leu	Leu Leu Thr Arg Gly Val	Asp Gly Ser Phe Leu Ala Arg	
20	25	30	
Pro Ser Lys	Ser Asn Pro Gly Asp Phe Thr Leu Ser Val Arg Arg Asn		
35	40	45	
Gly Ala Val	Thr His Ile Lys Ile Gln Asn Thr Gly Asp Tyr Tyr Asp		
50	55	60	
Leu Tyr Gly	Gly Glu Lys Phe Ala Thr Leu Ala Glu Leu Val Gln Tyr		
65	70	75	80
Tyr Met Glu	His His Gly Gln Leu Lys Glu Lys Asn Gly Asp Val Ile		
85	90	95	
Glu Leu Lys	Tyr Pro Leu Asn Cys Ala Asp Pro Thr Ser Glu Arg Trp		
100	105	110	
Phe His Gly	His Leu Ser Gly Lys Glu Ala Glu Lys Leu Leu Thr Glu		
115	120	125	
Lys Gly Lys	His Gly Ser Phe Leu Val Arg Glu Ser Gln Ser His Pro		
130	135	140	
Gly Asp Phe	Val Leu Ser Val Arg Thr Gly Asp Asp Lys Gly Glu Ser		
145	150	155	160
Asn Asp Gly	Lys Ser Lys Val Thr His Val Met Ile Arg Cys Gln Glu		
165	170	175	
Leu Lys Tyr	Asp Val Gly Gly Gly Glu Arg Phe Asp Ser Leu Thr Asp		
180	185	190	
Leu Val Glu	His Tyr Lys Lys Asn Pro Met Val Glu Thr Leu Gly Thr		
195	200	205	
Val Leu Gln	Leu Lys Gln Pro Leu Asn Thr Thr Arg Ile Asn Ala Ala		
210	215	220	
Glu Ile Glu	Ser Arg Val Arg Glu Leu Ser Lys Leu Ala Glu Thr Thr		
225	230	235	240
Asp Lys Val	Lys Gln Gly Phe Trp Glu Glu Phe Glu Thr Leu Gln Gln		
245	250	255	
Gln Glu Cys	Lys Leu Leu Tyr Ser Arg Lys Glu Gly Gln Arg Gln Glu		
260	265	270	
Asn Lys Asn	Lys Asn Arg Tyr Lys Asn Ile Leu Pro Phe Asp His Thr		
275	280	285	
Arg Val Val	Leu His Asp Gly Asp Pro Asn Glu Pro Val Ser Asp Tyr		
290	295	300	
Ile Asn Ala	Asn Ile Ile Met Pro Glu Phe Glu Thr Lys Cys Asn Asn		
305	310	315	320
Ser Lys Pro	Lys Lys Ser Tyr Ile Ala Thr Gln Gly Cys Leu Gln Asn		
325	330	335	
Thr Val Asn	Asp Phe Trp Arg Met Val Phe Gln Glu Asn Ser Arg Val		
340	345	350	
Ile Val Met	Thr Thr Lys Glu Val Glu Arg Gly Lys Ser Lys Cys Val		
355	360	365	
Lys Tyr Trp	Pro Asp Glu Tyr Ala Leu Lys Glu Tyr Gly Val Met Arg		
370	375	380	
Val Arg Asn	Val Lys Glu Ser Ala Ala His Asp Tyr Thr Leu Arg Glu		
385	390	395	400
Leu Lys Leu	Ser Lys Val Gly Gln Gly Asn Thr Glu Arg Thr Val Trp		
405	410	415	
Gln Tyr His	Phe Arg Thr Trp Pro Asp His Gly Val Pro Ser Asp Pro		
420	425	430	
Gly Gly Val	Leu Asp Phe Leu Glu Glu Val His His Lys Gln Glu Ser		
435	440	445	
Ile Met Asp	Ala Gly Pro Val Val Val His Cys Ser Ala Gly Ile Gly		
450	455	460	
Arg Thr Gly	Thr Phe Ile Val Ile Asp Ile Leu Ile Asp Ile Ile Arg		

465		470		475		480
Glu Lys Gly Val	Asp Cys Asp Ile	Asp Val Pro Lys Thr	Ile Gln Met			
	485	490	495			
Val Arg Ser Gln	Arg Ser Gly Met	Val Gln Thr Glu Ala	Gln Tyr Arg			
	500	505	510			
Phe Ile Tyr Met	Ala Val Gln His	Tyr Ile Glu Thr	Leu Gln Arg Arg			
	515	520	525			
Ile Glu Glu Glu	Gln Lys Ser Lys	Arg Lys Gly His	Glu Tyr Thr Asn			
	530	535	540			
Ile Lys Tyr Ser	Leu Ala Asp Gln	Thr Ser Gly Asp	Gln Ser Pro Leu			
545	550	555	560			
Pro Pro Cys Thr	Pro Thr Pro Cys	Ala Glu Met Arg	Glu Asp Ser			
	565	570	575			
Ala Arg Val Tyr	Glu Asn Val Gly	Leu Met Gln Gln	Gln Lys Ser Phe			
	580	585	590			

Arg

<210> 46
 <211> 2121
 <212> DNA
 <213> Homo sapiens

<400> 46

cgccaggcct	ggaggggggt	ctgtgcgcgg	ccggctggct	ctgccccgcg	tccggtcccg	60
agcgggcctc	cctcggggcca	gcccgatgtg	accgagccca	gcggagcctg	agcaaggagc	120
gggtccgtcg	cggagccgga	gggcgggagg	aacatgacat	cgcgagatg	gtttcaccca	180
aatatcactg	gtgtggaggc	agaaaaccta	ctgttgacaa	gaggagtga	tggcagtttt	240
ttggcaaggc	ctagtaaaag	taaccctgga	gacttcacac	tttccgttag	aagaaatgga	300
gctgtcacc	acatcaagat	tcagaacact	ggtgattact	atgacctgta	tggaggggag	360
aaatttgcca	ctttggctga	gttgggtccag	tattacatgg	aacatcacgg	gcaattaaaa	420
gagaagaatg	gagatgtcat	tgagcttaaa	tatcctctga	actgtgcaga	tcctacctct	480
gaaaggtgg	ttcatggaca	tctctctggg	aaagaagcag	agaaattatt	aactgaaaaa	540
ggaaaacatg	gtagttttct	tgtacgagag	agccagagcc	accctggaga	ttttgttctt	600
tctgtgcgca	ctgggtgatga	caaaggggag	agcaatgacg	gcaagtctaa	agtgacccat	660
gttatgattc	gctgtcagga	actgaaatac	gacgttggtg	gaggagaacg	gtttgattct	720
ttgacagatc	ttgtggaaca	ttataagaag	aatcctatgg	tggaaacatt	gggtacagta	780
ctacaactca	agcagcccct	taacacgact	cgtataaatg	ctgctgaaat	agaaagcaga	840
gttcgagaa	taagcaaatt	agctgagacc	acagataaag	tcaaacaagg	cttttgggaa	900
gaatttgaga	cactacaaca	acaggagtgc	aaacttctct	acagccgaaa	agaggggtcaa	960
aggcaagaaa	acaaaaacaa	aaatagatat	aaaaacatcc	tgccctttga	tcataccagg	1020
gttgtcctac	acgatgggtga	tcccaatgag	cctgtttcag	attacatcaa	tgcaaatatc	1080
atcatgcctg	aatttgaaac	caagtgcaac	aattcaaagc	ccaaaaagag	ttacattgcc	1140
acacaaggct	gcctgcaaaa	cacggtgaat	gacttttggc	ggatggtggt	ccaagaaaaa	1200
tcccagagtga	ttgtcatgac	aacgaaagaa	gtggagagag	gaaagagtaa	atgtgtcaaa	1260
tactggcctg	atgagtatgc	tctaaaagaa	tatggcgtca	tgctgttag	gaacgtcaaa	1320
gaaagcgccg	ctcatgacta	tacgctaaga	gaacttaaac	tttcaaagg	tggacaagg	1380
aatacggaga	gaacggctctg	gcaataccac	tttcggacct	ggccggacca	cggcgtgccc	1440
agcgaccctg	ggggcggtgc	ggacttctct	gaggaggtgc	accataagca	ggagagcatc	1500
atggatgcag	ggccggtcgt	ggtgcactgc	agtgtcggaa	ttggccggac	agggacgttc	1560
atttgtgattg	atattcttat	tgacatcatc	agagagaaag	gtgttgactg	cgatattgac	1620
gttcccaaaa	ccatccagat	ggtgcggtct	cagaggtcag	ggatgggtcca	gacagaagca	1680
cagtaccgat	ttatctatat	ggcgggtccag	cattatattg	aaacactaca	gcgcaggatt	1740
gaagaagagc	agaaaagcaa	gaggaaaggg	cacgaatata	caaataattaa	gtatttctcta	1800
gcggaccaga	cgagtggaga	tcagagccct	ctcccgccct	gtactccaac	gccaccctgt	1860
gcagaaatga	gagaagacag	tgctagagtc	tatgaaaacg	tgggcctgat	gcaacagcag	1920
aaaagtttca	gatgagaaaa	cctgccaata	cttcagcaca	gaaatagatg	tggactttca	1980

<400> 47

Met 1	Thr	Ser	Arg	Arg 5	Trp	Phe	His	Pro	Asn 10	Ile	Thr	Gly	Val	Glu 15	Ala
Glu	Asn	Leu	Leu	Leu	Thr	Arg	Gly	Val	Asp 25	Gly	Ser	Phe	Leu	Ala	Arg
Pro	Ser	Lys 35	Ser	Asn	Pro	Gly	Asp 40	Phe	Thr	Leu	Ser	Val 45	Arg	Arg	Asn
Gly	Ala 50	Val	Thr	His	Ile	Lys 55	Ile	Gln	Asn	Thr	Gly 60	Asp	Tyr	Tyr	Asp
Leu 65	Tyr	Gly	Gly	Glu	Lys 70	Phe	Ala	Thr	Leu	Ala 75	Glu	Leu	Val	Gln	Tyr 80
Tyr	Met	Glu	His	His 85	Gly	Gln	Leu	Lys 90	Glu	Lys	Asn	Gly	Asp 95	Val	Ile
Glu	Leu	Lys	Tyr 100	Pro	Leu	Asn	Cys 105	Ala	Asp	Pro	Thr	Ser 110	Glu	Arg	Trp
Phe	His	Gly 115	His	Leu	Ser	Gly	Lys 120	Glu	Ala	Glu	Lys	Leu 125	Leu	Thr	Glu
Lys	Gly 130	Lys	His	Gly	Ser	Phe 135	Leu	Val	Arg	Glu	Ser 140	Gln	Ser	His	Pro
Gly 145	Asp	Phe	Val	Leu	Ser 150	Val	Arg	Thr	Gly	Asp 155	Asp	Lys	Gly	Glu	Ser 160
Asn	Asp	Gly	Lys 165	Ser	Lys	Val	Thr	His 170	Val	Met	Ile	Arg 175	Cys	Gln	Glu
Leu	Lys	Tyr 180	Asp	Val	Gly	Gly	Gly 185	Glu	Arg	Phe	Asp	Ser 190	Leu	Thr	Asp
Leu	Val	Glu 195	His	Tyr	Lys	Lys	Asn 200	Pro	Met	Val	Glu	Thr 205	Leu	Gly	Thr
Val	Leu 210	Gln	Leu	Lys	Gln	Pro 215	Leu	Asn	Thr	Thr	Arg 220	Ile	Asn	Ala	Ala
Glu 225	Ile	Glu	Ser	Arg 230	Val	Arg	Glu	Leu	Ser	Lys 235	Leu	Ala	Glu	Thr	Thr 240
Asp	Lys	Val	Lys 245	Gln	Gly	Phe	Trp	Glu	Glu 250	Phe	Glu	Thr	Leu	Gln	Gln
Gln	Glu	Cys 260	Lys	Leu	Leu	Tyr	Ser 265	Arg	Lys	Glu	Gly	Gln 270	Arg	Gln	Glu
Asn	Lys 275	Asn	Lys	Asn	Arg	Tyr	Lys 280	Asn	Ile	Leu	Pro	Phe 285	Asp	His	Thr
Arg	Val 290	Val	Leu	His	Asp	Gly 295	Asp	Pro	Asn	Glu	Pro 300	Val	Ser	Asp	Tyr
Ile 305	Asn	Ala	Asn	Ile 310	Ile	Met	Pro	Glu	Phe 315	Glu	Thr	Lys	Cys	Asn	Asn 320
Ser	Lys	Pro	Lys 325	Lys	Ser	Tyr	Ile	Ala	Thr 330	Gln	Gly	Cys 335	Leu	Gln	Asn
Thr	Val	Asn 340	Asp	Phe	Trp	Arg	Met 345	Val	Phe	Gln	Glu	Asn 350	Ser	Arg	Val
Ile	Val 355	Met	Thr	Thr	Lys	Glu	Val 360	Glu	Arg	Gly	Lys 365	Ser	Lys	Cys	Val
Lys	Tyr 370	Trp	Pro	Asp	Glu	Tyr 375	Ala	Leu	Lys	Glu	Tyr 380	Gly	Val	Met	Arg

Val Arg Asn Val Lys Glu Ser Ala Ala His Asp Tyr Thr Leu Arg Glu
 385 390 395 400
 Leu Lys Leu Ser Lys Val Gly Gln Gly Asn Thr Glu Arg Thr Val Trp
 405 410 415
 Gln Tyr His Phe Arg Thr Trp Pro Asp His Gly Val Pro Ser Asp Pro
 420 425 430
 Gly Gly Val Leu Asp Phe Leu Glu Glu Val His His Lys Gln Glu Ser
 435 440 445
 Ile Met Asp Ala Gly Pro Val Val Val His Cys Ser Ala Gly Ile Gly
 450 455 460
 Arg Thr Gly Thr Phe Ile Val Ile Asp Ile Leu Ile Asp Ile Ile Arg
 465 470 475 480
 Glu Lys Gly Val Asp Cys Asp Ile Asp Val Pro Lys Thr Ile Gln Met
 485 490 495
 Val Arg Ser Gln Arg Ser Gly Met Val Gln Thr Glu Ala Gln Tyr Arg
 500 505 510
 Phe Ile Tyr Met Ala Val Gln His Tyr Ile Glu Thr Leu Gln Arg Arg
 515 520 525
 Ile Glu Glu Glu Gln Lys Ser Lys Arg Lys Gly His Glu Tyr Thr Asn
 530 535 540
 Ile Lys Tyr Ser Leu Ala Asp Gln Thr Ser Gly Asp Gln Ser Pro Leu
 545 550 555 560
 Pro Pro Cys Thr Pro Thr Pro Pro Cys Ala Glu Met Arg Glu Asp Ser
 565 570 575
 Ala Arg Val Tyr Glu Asn Val Gly Leu Met Gln Gln Gln Lys Ser Phe
 580 585 590
 Arg

<210> 48

<211> 1980

<212> DNA

<213> Homo sapiens

<400> 48

ggcacgagcg gctggctctg cccgcgtccg gtcccagagcg ggccctccctc gggccagccc 60
 gatgtgaccg agcccagcgg agcctgagca aggagcgggt ccgtcgcgga gccggaggggc 120
 gggaggaaca tgacatcgcg gagatggttt caccacaata tcaactggtgt ggaggcagaa 180
 aacctactgt tgacaagagg agttgatggc agtttttttg caaggcctag taaaagtaac 240
 cctggagact tcacactttc cgttagaaga aatggagctg tcacccacat caagattcag 300
 aacactggtg attactatga cctgtatgga ggggagaaat ttgccacttt ggctgagttg 360
 gtccagtatt acatggaaca tcacgggcaa ttaaagaga agaatggaga tgtcattgag 420
 cttaaataatc ctctgaactg tgcagatcct acctctgaaa ggtgggtttca tggacatctc 480
 tctgggaaag aagcagagaa attattaact gaaaaaggaa aacatggtag ttttcttgta 540
 cgagagagcc agagccaccc tggagatttt gttctttctg tgcgcactgg tgatgacaaa 600
 ggggagagca atgacggcaa gtctaaagtg acccatgtta tgattcgctg tcaggaaactg 660
 aaatacgacg ttggtggagg agaacggttt gattctttga cagatcttgt ggaacattat 720
 aagaagaatc ctatggtgga aacattgggt acagtactac aactcaagca gcccttaac 780
 acgactcgta taaatgctgc tgaatagctg tgggaagaat agcagagttc gagaactaag caaattagct 840
 gagaccacag ataaagtcaa acaaggcttt tgggaagaat ttgagacact acaacaacag 900
 gagtgc aaac ttctctacag ccgaaaagag ggtcaaaggc aagaaaacaa aaacaaaaat 960
 agatataaaa acatcctgcc ctttgatcat accagggttg tcctacacga tgggtgatccc 1020
 aatgagcctg tttcagatta catcaatgca aatatcatca tgccctgaatt tgaaaccaag 1080
 tgcaacaatt caaagcccaa aaagagttac attgccacac aaggctgcct gcaaaacacg 1140
 gtgaatgact tttggcggat ggtgttccaa gaaaactccc gagtgtattgt catgacaacg 1200
 aaagaagtgg agagaggaaa gagtaaattgt gtcaaatact ggccctgatga gtatgctcta 1260
 aaagaatatg gcgtcatgcg tgtaggaac gtcaaagaaa gcgccgctca tgactatacg 1320

```

ctaagagaac ttaaactttc aaaggttggg caaggggaata cggagagaac ggtctggcaa 1380
taccactttc ggacctggcc ggaccacggc gtgcccagcg accctggggg cgtgctggac 1440
ttcctggagg aggtgcacca taagcaggag agcatcatgg atgcagggcc ggtcgtggtg 1500
cactgcagtg ctggaattgg ccggacaggg acgttcattg tgattgatat tcttattgac 1560
atcatcagag agaaaggtgt tgactgcatg attgacgttc ccaaaacat ccagatggtg 1620
cggcttcaga ggtcagggat ggtccagaca gaagcacagt accgatttat ctatatggcg 1680
gtccagcatt atattgaaac actacagcgc aggattgaag aagagcagaa aagcaagagg 1740
aaagggcacg aatatacaaa tattaagtat tctctagcgg accagacgag tggagatcag 1800
agccctctcc cgccttgtag tccaacgcca ccctgtgcag aaatgagaga agacagtgtg 1860
agagtctatg aaaacgtggg cctgatgcaa cagcagaaaa gtttcagatg agaaaacctg 1920
ccaaaacttc agcacagaaa tagatgtgga ctttcacctc tccctaaaaa gatcaggacc 1980

```

<210> 49

<211> 584

<212> PRT

<213> Homo sapiens

<400> 49

```

Met Thr Ser Arg Arg Trp Phe His Pro Asn Ile Thr Gly Val Glu Ala
 1           5           10           15
Glu Asn Leu Leu Leu Thr Arg Gly Val Asp Gly Ser Phe Leu Ala Arg
      20           25           30
Pro Ser Lys Ser Asn Pro Gly Asp Phe Thr Leu Ser Val Arg Arg Asn
      35           40           45
Gly Ala Val Thr His Ile Lys Ile Gln Asn Thr Gly Asp Tyr Tyr Asp
      50           55           60
Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu Ala Glu Leu Val Gln Tyr
      65           70           75           80
Tyr Met Glu His His Gly Gln Leu Lys Glu Lys Asn Gly Asp Val Ile
      85           90           95
Glu Leu Lys Tyr Pro Leu Asn Cys Ala Asp Pro Thr Ser Glu Arg Trp
      100          105          110
Phe His Gly His Leu Ser Gly Lys Glu Ala Glu Lys Leu Leu Thr Glu
      115          120          125
Lys Gly Lys His Gly Ser Phe Leu Val Arg Glu Ser Gln Ser His Pro
      130          135          140
Gly Asp Phe Val Leu Ser Val Arg Thr Gly Asp Asp Lys Gly Glu Ser
      145          150          155          160
Asn Asp Gly Lys Ser Lys Val Thr His Val Met Ile Arg Cys Gln Glu
      165          170          175
Leu Lys Tyr Asp Val Gly Gly Gly Glu Arg Phe Asp Ser Leu Thr Asp
      180          185          190
Leu Val Glu His Tyr Lys Lys Asn Pro Met Val Glu Thr Leu Gly Thr
      195          200          205
Val Leu Gln Leu Lys Gln Pro Leu Asn Thr Thr Arg Ile Asn Ala Ala
      210          215          220
Glu Ile Glu Ser Arg Val Arg Glu Leu Ser Lys Leu Ala Glu Thr Thr
      225          230          235          240
Asp Lys Val Lys Gln Gly Phe Trp Glu Glu Phe Glu Thr Leu Gln Gln
      245          250          255
Gln Glu Cys Lys Leu Leu Tyr Ser Arg Lys Glu Gly Gln Arg Gln Glu
      260          265          270
Asn Lys Asn Lys Asn Arg Tyr Lys Asn Ile Leu Pro Phe Asp His Thr
      275          280          285
Arg Val Val Leu His Asp Gly Asp Pro Asn Glu Pro Val Ser Asp Tyr
      290          295          300
Ile Asn Ala Asn Ile Ile Met Pro Glu Phe Glu Thr Lys Cys Asn Asn

```


305						310						315						320
Ser	Lys	Pro	Lys	Lys	Ser	Tyr	Ile	Ala	Thr	Gln	Gly	Cys	Leu	Gln	Asn			
325					330					335								
Thr	Val	Asn	Asp	Phe	Trp	Arg	Met	Val	Phe	Gln	Glu	Asn	Ser	Arg	Val			
340					345					350								
Ile	Val	Met	Thr	Thr	Lys	Glu	Val	Glu	Arg	Gly	Lys	Ser	Lys	Cys	Val			
355					360					365								
Lys	Tyr	Trp	Pro	Asp	Glu	Tyr	Ala	Leu	Lys	Glu	Tyr	Gly	Val	Met	Arg			
370					375					380								
Val	Arg	Asn	Val	Lys	Glu	Ser	Ala	Ala	His	Asp	Tyr	Thr	Leu	Arg	Glu			
385					390					395								
Leu	Lys	Leu	Ser	Lys	Val	Gly	Gln	Gly	Asn	Thr	Glu	Arg	Thr	Val	Trp			
405					410					415								
Gln	Tyr	His	Phe	Arg	Thr	Trp	Pro	Asp	His	Gly	Val	Pro	Ser	Asp	Pro			
420					425					430								
Gly	Gly	Val	Leu	Asp	Phe	Leu	Glu	Glu	Val	His	His	Lys	Gln	Glu	Ser			
435					440					445								
Ile	Met	Asp	Ala	Gly	Pro	Val	Val	Val	His	Cys	Ser	Ala	Gly	Ile	Gly			
450					455					460								
Arg	Thr	Gly	Thr	Phe	Ile	Val	Ile	Asp	Ile	Leu	Ile	Asp	Ile	Ile	Arg			
465					470					475								
Glu	Lys	Gly	Val	Asp	Cys	Asp	Ile	Asp	Val	Pro	Lys	Thr	Ile	Gln	Met			
485					490					495								
Val	Arg	Ser	Gln	Arg	Ser	Gly	Met	Val	Gln	Thr	Glu	Ala	Gln	Tyr	Arg			
500					505					510								
Phe	Ile	Tyr	Met	Ala	Val	Gln	His	Tyr	Ile	Glu	Thr	Leu	Gln	Arg	Arg			
515					520					525								
Ile	Glu	Glu	Glu	Gln	Lys	Ser	Lys	Arg	Lys	Gly	His	Glu	Tyr	Thr	Asn			
530					535					540								
Ile	Lys	Tyr	Ser	Leu	Ala	Asp	Gln	Thr	Ser	Gly	Asp	Gln	Ser	Pro	Leu			
545					550					555								
Pro	Pro	Cys	Thr	Pro	Thr	Pro	Pro	Cys	Ala	Glu	Met	Arg	Glu	Asp	Ser			
565					570					575								
Ala	Arg	Val	Tyr	Glu	Asn	Val	Gly											
580																		

```
<210> 50
<211> 2338
<212> DNA
<213> Homo sapiens
```

<400>	50						
ggaggagcga	gccgggccgg	ggggcagctg	cacagtctcc	gggatcccca	ggcctggagg	60	
gggggtctgtg	cgcggccggc	tggctctgcc	ccgcgtccgg	tcccgagcgg	gcctccctcg	120	
ggccagcccg	atgtgaccga	gcccagcggg	gcctgagcaa	ggagcgggtc	cgtcgcggag	180	
ccggagggcg	ggaggaacat	gacatcgcgg	agatgggttc	acccaaatat	cactgggtgtg	240	
gaggcagaaa	acctactgtt	gacaagagga	gttgatggca	gttttttggc	aaggcctagt	300	
aaaagtaacc	ctggagactt	cacactttcc	gttagaagaa	atggagctgt	caccacatc	360	
aagattcaga	acactgggtga	ttactatgac	ctgtatggag	gggagaaatt	tgccactttg	420	
gctgagttgg	tccagtatta	catggaacat	cacgggcaat	taaaagagaa	gaatggagat	480	
gtcattgagc	ttaaatatcc	tctgaactgt	gcagatccta	cctctgaaag	gtggtttcat	540	
ggacactctct	ctgggaaaga	agcagagaaa	ttattaactg	aaaaaggaaa	acatggtagt	600	
tttcttgtac	gagagagcca	gagccaccct	ggagattttg	ttctttctgt	gcgcactggg	660	
gatgacaaag	ggagagagcaa	tgaccgcaag	tctaaagtga	cccatgttat	gattcgctgt	720	
caggaactga	aatacgacgt	tggctggagga	gaacgggttg	attctttgac	agatctttgt	780	
gaacattata	agaagaatcc	tatgggtggaa	acattgggta	cagtaactaca	actcaagcag	840	
cccttaaca	cgactcgtat	aaatgctgct	gaaatagaaa	gcagagttcg	agaaactaac	900	

```

aaattagctg agaccacaga taaagtcaaa caaggctttt gggaagaatt tgagacacta 960
caacaacagg agtgcaaaact tctctacagc cgaaaagagg gtcaaaggca agaaaacaaa 1020
aacaaaaata gatataaaaa catcctgccc tttgatcata ccagggttgt cctacacgat 1080
ggtgatccca atgagcctgt ttcagattac atcaatgcaa atatcatcat gcctgaattt 1140
gaaaccaagt gcaacaattc aaagcccaaa aagagttaca ttgccacaca aggctgcctg 1200
caaaacacgg tgaatgactt ttggcggatg gtgttccaag aaaactcccg agtgattgtc 1260
atgacaacga aagaagtgga gagaggaaag agtaaagtgt tcaaatactg gcctgatgag 1320
tatgctctaa aagaatatgg cgtcatgcgt gttaggaacg tcaaagaaag cgccgctcat 1380
gactatacgc taagagaact taaactttca aagggttgga aagggaatac ggagagaacg 1440
gtctggcaat accactttcg gacctggccg gaccacggcg tgcccagcga ccctgggggc 1500
gtgctggact tcctggagga ggtgcacat aagcaggaga gcatcatgga tgcaggggcg 1560
gtcgtggtgc actgcagtgc tgggaattggc cggacaggga cgttcattgt gattgatatt 1620
cttattgaca tcatcagaga gaaaggtgtt gactgcgata ttgacgttcc caaaaccatc 1680
cagatggtgc ggtctcagag gtcagggatg gtccagacag aagcacagta ccgattttatc 1740
tatatggcgg tccagcatta tattgaaaca ctacagcgca ggattgaaga agagcagaaa 1800
agcaagagga aagggcacga atatacaaat attaagtatt ctctagcgga ccagacgagt 1860
ggagatcaga gccctctccc gccttgatc ccaacgccac cctgtgcaga aatgagagaa 1920
gacagtgcga gagtctatga aaacgtgggc ctgatgcaac agcagaaaag tttcagatga 1980
gaaaacctgc caaaaacttca gcacagaaat agatgtggac tttcacctc tccttaaaaa 2040
gatcaagaac agacgcaaga aagtttatgt gaagacagaa tttggatttg ggaaggcttg 2100
caatgtggtt gactaccttt tgataagcaa aatttgaaac catttaaga ccactgtatt 2160
ttaactcaac aatacctgct tccaattac tcatttctc agataagaag aaatcatctc 2220
tacaatgtag acaacattat attttataga atttgttga aattgaggaa gcagttaaat 2280
tgtgcgctgt attttgcaga ggattatggg gattcaaatt ctagtaatag gccttttt 2338

```

<210> 51

<211> 274

<212> DNA

<213> Homo sapiens

<400> 51

```

cagtactggc ctgatgagta tgctctaaaa gaatatggcg tcatgcgtgt taggaacgtc 60
aaagaaagcg ccgctcatga ctatacgcta agagaactta aactttcaaa ggttggacaa 120
gggaatacgg agagaacggt ctggcaatac cactttcgga cctggccgga ccacggcgtg 180
cccagcgacc ctgggggcgt gctggacttc ctggaggagg tgcaccataa gcaggagagc 240
atcatggatg cagggccggt cgtggtgcac tgca 274

```

<210> 52

<211> 91

<212> PRT

<213> Homo sapiens

<400> 52

```

Gln Tyr Trp Pro Asp Glu Tyr Ala Leu Lys Glu Tyr Gly Val Met Arg
1           5           10           15
Val Arg Asn Val Lys Glu Ser Ala Ala His Asp Tyr Thr Leu Arg Glu
20           25           30
Leu Lys Leu Ser Lys Val Gly Gln Gly Asn Thr Glu Arg Thr Val Trp
35           40           45
Gln Tyr His Phe Arg Thr Trp Pro Asp His Gly Val Pro Ser Asp Pro
50           55           60
Gly Gly Val Leu Asp Phe Leu Glu Glu Val His Lys Gln Glu Ser
65           70           75           80
Ile Met Asp Ala Gly Pro Val Val Val His Cys
85           90

```

<210> 53

<211> 90
 <212> DNA
 <213> Homo sapiens

<400> 53
 acggagagaa cggctctggca ataccacttt cggacctggc cggaccacgg cgtgcccagc 60
 gacctgggg gcgtgctgga cttcctggag 90

<210> 54
 <211> 2229
 <212> DNA
 <213> Mus musculus

<400> 54
 ggtacccgc ggagcctgag cgagcaggcg tccgtgcgga gccgaagacg ggaggaacat 60
 gacatcgcg agatggtttc accccaacat cactggtgtg gaggcagaga atctcctgct 120
 gaccagagga gtcgatggca gtttttttagc aaggccagc aagagtaacc ctggagactt 180
 cactctgtct gttagaagaa atggagctgt taccacatc aagattcaga aactgggga 240
 ctactatgac ctctatggtg gggagaagtt tgccactttg gctgaactgg ttcagtatta 300
 catggaacac catgggcagc tgaaagagaa gaatggagat gttatcgagc tcaagtacc 360
 gctgaactgt gcagacccta cctctgaaag gtggttccat ggtcacttgt ctggaaaaga 420
 agcagagaag ctgctgacgg agaagggcaa gcacggcagc ttcctcgttc gagagagcca 480
 gagccacccc ggagacttctg ttctctccgt gcgactggt gagacaaaag gggagagcaa 540
 cgacggcaag tccaaagtga cccacgtcat gatccgctgt caggagctga aatacgacgt 600
 tgggtggggga gagcgctttg actctctgac agacctggtg gagcattaca agaagaacct 660
 catggtggag acgctgggca cagtcctgca gctcaagcag cccctcaaca caactcgtat 720
 caatgctgct gaaattgaaa gccgggttcg agagttaagc aagctggctg agaccacaga 780
 taaagtcaag cagggctttt gggaagagtt tgagacgctc cagcaacagg aatgcaaaact 840
 tctctatagc cgaaaagaag gacagagaca agaaaataaa acaaaaaaca gatacaaaaa 900
 catcctgccc tttgatcata ccagggtcgt tctgcatgat ggggatccca atgagcctgt 960
 ttctgattac attaatgcaa acatcatcat gctgagttt gagaccaagt gcaacaattc 1020
 caaacccaaa aagagttaca ttgccactca aggtgctctg cagaacacgg tgaatgactt 1080
 ctggcggtatg gtgttccagg agaactctcg agtcattgtc atgaccacaa aggaagtgga 1140
 gagaggggaag agcaaatgtg tcaagtactg gcctgatgag tatgcgctca aagaatacgg 1200
 ggtcatgctg gttaggaacg tcaaagaaag tgccgcccac gactacactt tacgagagct 1260
 caaactctct aaggtcggac aagctctact ccagggaac acagagagaa ccgtctggca 1320
 gtaccacttt cggacctggc cagaccatgg cgtgcctagt gacctggag gtgtgctgga 1380
 cttcctggag gaggtccacc acaagcagga gagcatcgtg gatgcaggcc ctgtcgtggt 1440
 tctactgcagc gctgggattg gccggacagg aaccttcatt gtgattgaca tctttattga 1500
 catcattcga gagaaagggtg tggactgtga catcgacgtt cctaaaacca ttcagatggt 1560
 gcggtcccag aggtcgggga tgggtccagac agaagcacag taccggttta tctacatggc 1620
 tgtccagcac tacatagaga cgctgcagcg ccggatcgag gaggagcaga aaagcaaaag 1680
 aaaaggacat gaatatacca atattaagta ttcttgggtg gaccagacaa gtggtgatca 1740
 gagtccctg ccaccctgca cccaacgcc acctgtgca gaaatgaggg aggacagcgc 1800
 ccgagtctat gagaacgtgg gcctcatgca gcagcagagg agtttcagat gagccacgg 1860
 cgacagaacg cagatgtgaa ctttcacccc ttctctaaaa tgtcaagact agacgagcgt 1920
 tcccaggacc cgtgcgtgag ttcagaagcc ggactggct ggactgcctc ttgagaagcg 1980
 aagtttgga ccatttgaa agcacgtgcc taattggcac ctctttctc cagctaagga 2040
 gagactgctc tgcgttcttg acaatgctat ttgctagaa ttggttttga attgtggaag 2100
 cagctaaatt gtgctctgta ttttctacat tatgggactc aaattctagt tatgggcagg 2160
 attttgtttc tttttatgac cttaacagat ctgatttttt ttttctttct ctctctttgg 2220
 ggaatcatg 2229

<210> 55
 <211> 597
 <212> PRT
 <213> Mus musculus

<400> 55

```

Met Thr Ser Arg Arg Trp Phe His Pro Asn Ile Thr Gly Val Glu Ala
 1          5          10          15
Glu Asn Leu Leu Leu Thr Arg Gly Val Asp Gly Ser Phe Leu Ala Arg
          20          25          30
Pro Ser Lys Ser Asn Pro Gly Asp Phe Thr Leu Ser Val Arg Arg Asn
          35          40          45
Gly Ala Val Thr His Ile Lys Ile Gln Asn Thr Gly Asp Tyr Tyr Asp
          50          55          60
Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu Ala Glu Leu Val Gln Tyr
65          70          75          80
Tyr Met Glu His His Gly Gln Leu Lys Glu Lys Asn Gly Asp Val Ile
          85          90          95
Glu Leu Lys Tyr Pro Leu Asn Cys Ala Asp Pro Thr Ser Glu Arg Trp
          100          105          110
Phe His Gly His Leu Ser Gly Lys Glu Ala Glu Lys Leu Leu Thr Glu
          115          120          125
Lys Gly Lys His Gly Ser Phe Leu Val Arg Glu Ser Gln Ser His Pro
          130          135          140
Gly Asp Phe Val Leu Ser Val Arg Thr Gly Asp Asp Lys Gly Glu Ser
145          150          155          160
Asn Asp Gly Lys Ser Lys Val Thr His Val Met Ile Arg Cys Gln Glu
          165          170          175
Leu Lys Tyr Asp Val Gly Gly Gly Glu Arg Phe Asp Ser Leu Thr Asp
          180          185          190
Leu Val Glu His Tyr Lys Lys Asn Pro Met Val Glu Thr Leu Gly Thr
          195          200          205
Val Leu Gln Leu Lys Gln Pro Leu Asn Thr Thr Arg Ile Asn Ala Ala
          210          215          220
Glu Ile Glu Ser Arg Val Arg Glu Leu Ser Lys Leu Ala Glu Thr Thr
225          230          235          240
Asp Lys Val Lys Gln Gly Phe Trp Glu Glu Phe Glu Thr Leu Gln Gln
          245          250          255
Gln Glu Cys Lys Leu Leu Tyr Ser Arg Lys Glu Gly Gln Arg Gln Glu
          260          265          270
Asn Lys Asn Lys Asn Arg Tyr Lys Asn Ile Leu Pro Phe Asp His Thr
          275          280          285
Arg Val Val Leu His Asp Gly Asp Pro Asn Glu Pro Val Ser Asp Tyr
          290          295          300
Ile Asn Ala Asn Ile Ile Met Pro Glu Phe Glu Thr Lys Cys Asn Asn
305          310          315          320
Ser Lys Pro Lys Lys Ser Tyr Ile Ala Thr Gln Gly Cys Leu Gln Asn
          325          330          335
Thr Val Asn Asp Phe Trp Arg Met Val Phe Gln Glu Asn Ser Arg Val
          340          345          350
Ile Val Met Thr Thr Lys Glu Val Glu Arg Gly Lys Ser Lys Cys Val
          355          360          365
Lys Tyr Trp Pro Asp Glu Tyr Ala Leu Lys Glu Tyr Gly Val Met Arg
370          375          380
Val Arg Asn Val Lys Glu Ser Ala Ala His Asp Tyr Thr Leu Arg Glu
385          390          395          400
Leu Lys Leu Ser Lys Val Gly Gln Ala Leu Leu Gln Gly Asn Thr Glu
          405          410          415
Arg Thr Val Trp Gln Tyr His Phe Arg Thr Trp Pro Asp His Gly Val
          420          425          430
Pro Ser Asp Pro Gly Gly Val Leu Asp Phe Leu Glu Glu Val His His
          435          440          445
Lys Gln Glu Ser Ile Val Asp Ala Gly Pro Val Val Val His Cys Ser

```

450	455	460
Ala Gly Ile Gly Arg Thr Gly Thr Phe Ile Val Ile Asp Ile Leu Ile		
465	470	475
Asp Ile Ile Arg Glu Lys Gly Val Asp Cys Asp Ile Asp Val Pro Lys		480
	485	490
Thr Ile Gln Met Val Arg Ser Gln Arg Ser Gly Met Val Gln Thr Glu		495
	500	505
Ala Gln Tyr Arg Phe Ile Tyr Met Ala Val Gln His Tyr Ile Glu Thr		510
	515	520
Leu Gln Arg Arg Ile Glu Glu Glu Gln Lys Ser Lys Arg Lys Gly His		525
	530	535
Glu Tyr Thr Asn Ile Lys Tyr Ser Leu Val Asp Gln Thr Ser Gly Asp		540
545	550	555
Gln Ser Pro Leu Pro Pro Cys Thr Pro Thr Pro Pro Cys Ala Glu Met		560
	565	570
Arg Glu Asp Ser Ala Arg Val Tyr Glu Asn Val Gly Leu Met Gln Gln		575
	580	585
Gln Arg Ser Phe Arg		590
595		

<210> 56

<211> 2236

<212> DNA

<213> Rattus norvegicus

<400> 56

```

cgggctcccc agcggggcct cactcggccc cctccatgtg acgggcgcctc gtggagcctg 60
agtgagcagc ggggtccgtgc ggagccggag gcgggaggaa catgacatcc cggagatggg 120
ttcaccccaa tactactggg gtggaggcag agaattctct gctgacccca ggagtcgatg 180
gcagtttctt agcggagccc agcaagagta accctggaga cttcactctg tctgttagaa 240
gaaatggagc cggtaccac atcaagattc agaacactgg ggactactat gacctctatg 300
gcggggaaaa gtttgccacc ttgcctgaac tgggtccagta ttacatggag catcacgggc 360
agctgaaaga gaagaatgga gatgttattg agctcaagta cccactgaac tgtgcagacc 420
ctacctctga aaggtgggtc cacgggtcact tgtctggaaa agaagcagag aagctgctga 480
cagagaaggg gaagcatggc agtttctctc tccgggagag ccagagccac cctggggact 540
tcgtcctctc cgtccgcgat ggtgatgaca aaggggagag caatgacagc aagtccaaag 600
tgacctatgt catgatccgc tgtcaggagc tgaatatga tgttggtgga ggagagcgct 660
ttgactcttt gacagacctg gtggagcatt acaagaagaa ccccatgggt gagacactgg 720
gcacagtccg gcagctcaaa cagccctca acacaactcg tattaatgcc gctgaaatcg 780
aaagccgggt tcgggagtta agcaagctag ccgagaccac agataaagtc aaacagggct 840
tttgggaaga atttgagact ctacagcaac aggaatgcaa acttctctac agccgaaaag 900
aaggacagag acaagaaaat aaaaacaaaa atagatacaa aaacatcctg ccctttgatc 960
ataccagggt tgtcctgcac gatggggatc ccaacgagcc agtttctgat tacatcaatg 1020
ccaacatcat catgcctgaa tttgaaacca agtgcaacaa ttcaaaaccc aaaaagagtt 1080
acattgccac tcaaggctgc ctgcagaaca cgggtgaatga cttctggcgg atggtgttcc 1140
aggagaactc tcgagtcatt gtcatgacca caaaggaagt ggagagaggg aagagcaagt 1200
gtgtcaagta ctggcctgat gagtgtgcac tcaaagagta tggcgatcat cgtgtgagga 1260
acgtcagaga aagtgtgcg catgactaca ccttacgaga actcaaactc tctaaggctc 1320
gacaaggaaa cacagagaga accgtctggc agtaccactt tcggacctgg ccagaccacg 1380
gtgtgcctag tgacctgga ggtgtgctgg acttctctga ggaggtccac cacaagcagg 1440
agagcatcgt ggatgcaggc cctgtcgtgg ttactgcag tgcctgggatt ggccggacag 1500
gaacgttcat tgtgattgat atccttattg acatcatccg agagaaaggt gtggactgtg 1560
acatcgacgt tcctaaaacc attcagatgg tacgggtccc gaggtcaggg atggtccaga 1620
cagaagcaca gtaccggttc atctacatgg ccgtccagca ctacatagag acgctgcaac 1680
gcaggatcga ggaggagcag aaaagcaaaa ggaaaggaca tgaatatacc aatattaagt 1740
attccctggg ggaccagaca agtggcgatc agagtccct gccaccttgc accccaacgc 1800
cacctgtgc ggaaatgcgg gaggacagcg ctcgagtcta tgagaacgtg ggcctcatgc 1860

```

```

agcagcagag gagtttcaga tgagcttcgg gtggcagcgc gcagatgtga actttcaccc 1920
cttcctctaaa atgtcaagaa tagacgagaa agttttccagg acccgtgttc agaagctcgc 1980
cgggggttgac tgactgcctt ttgagaagcg aagtttggaa ccatttgaaa gagcacgtgc 2040
ctaattggca cctcctttcc tcagctaagg agaaactgct ctgcgttgtc gacagtgtga 2100
ttgtcatgga attggttttg aattgtgaag cagctaaatt gtgctctgta ttttctacat 2160
tgtgggactc aaattctagt cacgggcagg attttgttg tttcttttta tgacctaac 2220
agacctgtta agaccg                                     2236

```

<210> 57

<211> 583

<212> PRT

<213> Rattus norvegicus

<400> 57

```

Met Thr Ser Arg Arg Trp Phe His Pro Asn Ile Thr Gly Val Glu Ala
 1          5          10          15
Glu Asn Leu Leu Leu Thr Arg Gly Val Asp Gly Ser Phe Leu Ala Arg
          20          25          30
Pro Ser Lys Ser Asn Pro Gly Asp Phe Thr Leu Ser Val Arg Arg Asn
          35          40          45
Gly Ala Val Thr His Ile Lys Ile Gln Asn Thr Gly Asp Tyr Tyr Asp
          50          55          60
Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu Pro Glu Leu Val Gln Tyr
65          70          75          80
Tyr Met Glu His His Gly Gln Leu Lys Glu Lys Asn Gly Asp Val Ile
          85          90          95
Glu Leu Lys Tyr Pro Leu Asn Cys Ala Asp Pro Thr Ser Glu Arg Trp
          100          105          110
Phe His Gly His Leu Ser Gly Lys Glu Ala Glu Lys Leu Leu Thr Glu
          115          120          125
Lys Gly Lys His Gly Ser Phe Leu Val Arg Glu Ser Gln Ser His Pro
          130          135          140
Gly Asp Phe Val Leu Ser Val Arg Thr Gly Asp Asp Lys Gly Glu Ser
145          150          155          160
Asn Asp Ser Lys Ser Lys Val Thr His Val Met Ile Arg Cys Gln Glu
          165          170          175
Leu Lys Tyr Asp Val Gly Gly Gly Glu Arg Phe Asp Ser Leu Thr Asp
          180          185          190
Leu Val Glu His Tyr Lys Lys Asn Pro Met Val Glu Thr Leu Gly Thr
          195          200          205
Val Leu Gln Leu Lys Gln Pro Leu Asn Thr Thr Arg Ile Asn Ala Ala
          210          215          220
Glu Ile Glu Ser Arg Val Arg Glu Leu Ser Lys Leu Ala Glu Thr Thr
225          230          235          240
Asp Lys Val Lys Gln Gly Phe Trp Glu Glu Phe Glu Thr Leu Gln Gln
          245          250          255
Gln Glu Cys Lys Leu Leu Tyr Ser Arg Lys Glu Gly Gln Arg Gln Glu
          260          265          270
Asn Lys Asn Lys Asn Arg Tyr Lys Asn Ile Leu Pro Phe Asp His Thr
          275          280          285
Arg Val Val Leu His Asp Gly Asp Pro Asn Glu Pro Val Ser Asp Tyr
          290          295          300
Ile Asn Ala Asn Ile Ile Met Pro Glu Phe Glu Thr Lys Cys Asn Asn
305          310          315          320
Ser Lys Pro Lys Lys Ser Tyr Ile Ala Thr Gln Gly Cys Leu Gln Asn
          325          330          335
Thr Val Asn Asp Phe Trp Arg Met Val Phe Gln Glu Asn Ser Arg Val
          340          345          350

```

Ile Val Met Thr Thr Lys Glu Val Glu Arg Gly Lys Ser Lys Cys Val
 355 360 365
 Lys Tyr Trp Pro Asp Glu Cys Ala Leu Lys Glu Tyr Gly Val Met Arg
 370 375 380
 Val Arg Asn Val Arg Glu Ser Ala Ala His Asp Tyr Thr Leu Arg Glu
 385 390 395 400
 Leu Lys Leu Ser Lys Val Gly Gln Gly Asn Thr Glu Arg Thr Val Trp
 405 410 415
 Gln Tyr His Phe Arg Thr Trp Pro Asp His Gly Val Pro Ser Asp Pro
 420 425 430
 Gly Gly Val Leu Asp Phe Leu Glu Glu Val His His Lys Gln Glu Ser
 435 440 445
 Ile Val Asp Ala Gly Pro Val Val Val His Cys Ser Ala Gly Ile Gly
 450 455 460
 Arg Thr Gly Thr Phe Ile Val Ile Asp Ile Leu Ile Asp Ile Ile Arg
 465 470 475 480
 Glu Lys Gly Val Asp Cys Asp Ile Asp Val Pro Lys Thr Ile Gln Met
 485 490 495
 Val Arg Ser Gln Arg Ser Gly Met Val Gln Thr Glu Ala Gln Tyr Arg
 500 505 510
 Phe Ile Tyr Met Ala Val Gln His Tyr Ile Glu Thr Leu Gln Arg Arg
 515 520 525
 Ile Glu Glu Glu Gln Lys Ser Lys Arg Lys Gly His Glu Tyr Thr Asn
 530 535 540
 Ile Lys Tyr Ser Leu Val Asp Gln Thr Ser Gly Asp Gln Ser Pro Leu
 545 550 555 560
 Pro Pro Cys Thr Pro Thr Pro Pro Cys Ala Glu Met Arg Glu Asp Ser
 565 570 575
 Ala Arg Val Tyr Glu Asn Val
 580

<210> 58
 <211> 2090
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 2090
 <223> n = A,T,C or G

<400> 58
 cttagtccct gagctctctg cctgcccaga ctagctgcac ctctcattc cctgcgcccc 60
 cttcctctcc ggaagcccc aggatggtga ggtggtttca ccgagacctc agtgggctgg 120
 atgcagagac cctgctcaag ggccgagggtg tccacggtag cttcctggct cggcccagtc 180
 gcaagaacca gggtgacttc tcgctctccg tcaggggtggg ggatcagggtg acccatattc 240
 ggatccagaa ctcaggggat ttctatgacc tgtatggagg ggagaagttt gcgactctga 300
 cagagctggt ggagtactac actcagcagc aggggtgtct gcaggaccgc gacggcacca 360
 tcatccacct caagtaccgc ctgaactgct ccgatccac tagtgagagg tggtaccatg 420
 gccacatgtc tggcgggcag gcagagacgc tgctgcaggc caagggcgag ccctggacgt 480
 ttcttgtgcg tgagagcctc agccagcctg gagacttcgt gctttctgtg ctcagtgacc 540
 agcccaaggc tggcccaggc tccccgctca gggtcaccac catcaaggtc atgtgcgagg 600
 gtggacgcta cacagtgggt ggtttggaga ccttcgacag cctcacggac ctggtggagc 660
 atttcaagaa gacggggatt gaggaggcct caggcgcctt tgtctacctg cggcagccgt 720
 actatgccac gagggtgaat gcggctgaca ttgagaaccg agtggttgaa ctgaacaaga 780
 agcaggagtc cgaggatata gccaaaggctg gcttctggga ggagtttgag agtttgcaga 840
 agcaggaggt gaagaacttg caccagcgtc tggaagggca gcggccagag aacaagggca 900

```

agaaccgcta caagaacatt ctcccctttg accacagccg agtgatcctg cagggacggg 960
acagtaacat ccccggttcc gactacatca atgccaacta catcaagaac cagctgctag 1020
gccctgatga gaacgctaag acctacatcg ccagccaggg ctgtctggag gccacggtca 1080
atgacttctg gcagatggcg tggcaggaga acagccgtgt catcgtcag accacccgag 1140
aggtggagaa aggccggaac aaatgcgtcc catactggcc cgaggtgggc atgcagcgtg 1200
cttatgggcc ctactctgtg accaactgcg gggagcatga cacaaccgaa taaaactcc 1260
gtaccttaca ggtctccccg ctggacaatg gagacctgat tggggagatc tggcattacc 1320
agtacctgag ctggcccgac catggggtcc ccagttagcc tgggggtgtc ctcagcttcc 1380
tggaccagat caaccagcgg caggaaagtc tgcctcacgc agggcccatc atcgtgcact 1440
gcagcgccgg catcgccgc acaggcacca tcattgtcat cgacatgctc atggagaaca 1500
tctccaccaa gggcctggac tgtgacattg acatccagaa gaccatccag atgggtgcggg 1560
cgcagcgctc gggcatggtg cagacggagg cgagtagaa gttcatctac gtggccatcg 1620
cccagttcat tgaaccact aagaagaagc tggaggtcct gcagtcgcag aagggccagg 1680
agtcggagta cggaacatc acctatcccc cagccatgaa gaatgccat gccaaaggcct 1740
cccgcacctc gtccaaacac aaggaggatg tgtatgagaa cctgcacact aagaacaaga 1800
gggaggagaa agtgaagaag cagcggtcag cagacaagga gaagagcaag ggttccctca 1860
agaggaagtg agcggtgctg tctcaggtg gccatgcctc agccctgacc ctgtggaagg 1920
atttcgcgat ggacagactc acaacctgaa cctaggagat gtcgtattct tttgtaattt 1980
aaatggctgt atcccccccc taacctctcc ctgaccctgt atatagccca gccaggccca 2040
gcagggccac ccttctcctc ttgtaaataa agccctggga tcactgtgan 2090

```

<210> 59

<211> 595

<212> PRT

<213> Homo sapiens

<400> 59

```

Met Val Arg Trp Phe His Arg Asp Leu Ser Gly Leu Asp Ala Glu Thr
 1           5           10           15
Leu Leu Lys Gly Arg Gly Val His Gly Ser Phe Leu Ala Arg Pro Ser
 20           25           30
Arg Lys Asn Gln Gly Asp Phe Ser Leu Ser Val Arg Val Gly Asp Gln
 35           40           45
Val Thr His Ile Arg Ile Gln Asn Ser Gly Asp Phe Tyr Asp Leu Tyr
 50           55           60
Gly Gly Glu Lys Phe Ala Thr Leu Thr Glu Leu Val Glu Tyr Tyr Thr
 65           70           75           80
Gln Gln Gln Gly Val Leu Gln Asp Arg Asp Gly Thr Ile Ile His Leu
 85           90           95
Lys Tyr Pro Leu Asn Cys Ser Asp Pro Thr Ser Glu Arg Trp Tyr His
100           105           110
Gly His Met Ser Gly Gly Gln Ala Glu Thr Leu Leu Gln Ala Lys Gly
115           120           125
Glu Pro Trp Thr Phe Leu Val Arg Glu Ser Leu Ser Gln Pro Gly Asp
130           135           140
Phe Val Leu Ser Val Leu Ser Asp Gln Pro Lys Ala Gly Pro Gly Ser
145           150           155           160
Pro Leu Arg Val Thr His Ile Lys Val Met Cys Glu Gly Gly Arg Tyr
165           170           175
Thr Val Gly Gly Leu Glu Thr Phe Asp Ser Leu Thr Asp Leu Val Glu
180           185           190
His Phe Lys Lys Thr Gly Ile Glu Glu Ala Ser Gly Ala Phe Val Tyr
195           200           205
Leu Arg Gln Pro Tyr Tyr Ala Thr Arg Val Asn Ala Ala Asp Ile Glu
210           215           220
Asn Arg Val Leu Glu Leu Asn Lys Lys Gln Glu Ser Glu Asp Thr Ala
225           230           235           240
Lys Ala Gly Phe Trp Glu Glu Phe Glu Ser Leu Gln Lys Gln Glu Val

```


					245					250					255
Lys	Asn	Leu	His	Gln	Arg	Leu	Glu	Gly	Gln	Arg	Pro	Glu	Asn	Lys	Gly
			260					265					270		
Lys	Asn	Arg	Tyr	Lys	Asn	Ile	Leu	Pro	Phe	Asp	His	Ser	Arg	Val	Ile
		275					280					285			
Leu	Gln	Gly	Arg	Asp	Ser	Asn	Ile	Pro	Gly	Ser	Asp	Tyr	Ile	Asn	Ala
		290				295					300				
Asn	Tyr	Ile	Lys	Asn	Gln	Leu	Leu	Gly	Pro	Asp	Glu	Asn	Ala	Lys	Thr
305					310					315					320
Tyr	Ile	Ala	Ser	Gln	Gly	Cys	Leu	Glu	Ala	Thr	Val	Asn	Asp	Phe	Trp
				325					330					335	
Gln	Met	Ala	Trp	Gln	Glu	Asn	Ser	Arg	Val	Ile	Val	Met	Thr	Thr	Arg
			340					345					350		
Glu	Val	Glu	Lys	Gly	Arg	Asn	Lys	Cys	Val	Pro	Tyr	Trp	Pro	Glu	Val
		355					360					365			
Gly	Met	Gln	Arg	Ala	Tyr	Gly	Pro	Tyr	Ser	Val	Thr	Asn	Cys	Gly	Glu
		370				375					380				
His	Asp	Thr	Thr	Glu	Tyr	Lys	Leu	Arg	Thr	Leu	Gln	Val	Ser	Pro	Leu
385					390					395					400
Asp	Asn	Gly	Asp	Leu	Ile	Arg	Glu	Ile	Trp	His	Tyr	Gln	Tyr	Leu	Ser
				405					410					415	
Trp	Pro	Asp	His	Gly	Val	Pro	Ser	Glu	Pro	Gly	Gly	Val	Leu	Ser	Phe
			420					425					430		
Leu	Asp	Gln	Ile	Asn	Gln	Arg	Gln	Glu	Ser	Leu	Pro	His	Ala	Gly	Pro
		435					440					445			
Ile	Ile	Val	His	Cys	Ser	Ala	Gly	Ile	Gly	Arg	Thr	Gly	Thr	Ile	Ile
		450				455					460				
Val	Ile	Asp	Met	Leu	Met	Glu	Asn	Ile	Ser	Thr	Lys	Gly	Leu	Asp	Cys
465					470					475					480
Asp	Ile	Asp	Ile	Gln	Lys	Thr	Ile	Gln	Met	Val	Arg	Ala	Gln	Arg	Ser
				485					490					495	
Gly	Met	Val	Gln	Thr	Glu	Ala	Gln	Tyr	Lys	Phe	Ile	Tyr	Val	Ala	Ile
			500					505					510		
Ala	Gln	Phe	Ile	Glu	Thr	Thr	Lys	Lys	Lys	Leu	Glu	Val	Leu	Gln	Ser
		515					520					525			
Gln	Lys	Gly	Gln	Glu	Ser	Glu	Tyr	Gly	Asn	Ile	Thr	Tyr	Pro	Pro	Ala
		530				535					540				
Met	Lys	Asn	Ala	His	Ala	Lys	Ala	Ser	Arg	Thr	Ser	Ser	Lys	His	Lys
545					550					555					560
Glu	Asp	Val	Tyr	Glu	Asn	Leu	His	Thr	Lys	Asn	Lys	Arg	Glu	Glu	Lys
				565					570					575	
Val	Lys	Lys	Gln	Arg	Ser	Ala	Asp	Lys	Glu	Lys	Ser	Lys	Gly	Ser	Leu
			580					585							

<210> 60

<211> 2277

<212> DNA

<213> Homo sapiens

<400> 60

caagaagacg	gggattgagg	aggcctcagg	cgctttgtc	tacctgcggc	agccgtacta	60
tgccacgagg	gtgaatgcgg	ctgacattga	gaaccgagtg	ttggaactga	acaagaagca	120
ggagtccgag	gaggaagtgg	ctgattactg	agcggttctt	cctcacctgg	cttggggcac	180
tgtgcacagc	tgtgccgctg	gctcagcccc	gccccctgcg	gccctccgcc	gtggcttccc	240
cctccctaca	gagagatgct	gtcccggtggg	tggtttcacc	gagacctcag	tgggctggat	300

```

gcagagaccc tgctcaaggg ccgaggtgtc cacggtagct tcctggctcg gcccagtcgc 360
aagaaccagg gtgacttctc gctctccgtc aggggtgggg atcaggtgac ccatattcgg 420
atccagaact caggggattt ctatgacctg tatggagggg agaagtttgc gactctgaca 480
gagctggttg agtactacac tcagcagcag ggtgtcctgc aggaccgcga cggcaccatc 540
atccacctca agtaccctgt gaactgctcc gatcccacta gtgagaggtg gtaccatggc 600
cacatgtctg gcgggcaggc agagacgctg ctgcaggcca agggcgagcc ctggacgttt 660
cttgtgctg agagcctcag ccagcctgga gacttcgtgc tttctgtgct cagtgaccag 720
cccaaggctg gccaggctc cccgctcagg gtcacccaca tcaaggtcat gtgcgagggt 780
ggacgctaca cagtgggttg tttggagacc ttcgacagcc tcacggacct ggtagagcat 840
ttcaagaaga cggggattga ggaggcctca ggcgcctttg tctacctgcg gcagccgtac 900
tatgccacga ggggtgaatgc ggctgacatt gagaaccgag tgttggaaact gaacaagaag 960
caggagtccg aggatacagc caaggctggc ttctgggagg agtttgagag tttgcagaag 1020
caggaggtga agaacttgca ccagcgtctg gaagggcagc ggccagagaa caagggcaag 1080
aaccgctaca agaacttct cccctttgac cacagccgag tgatcctgca gggacgggac 1140
agtaacatcc ccgggtccga ctacatcaat gccaaactaca tcaagaacca gctgctaggc 1200
cctgatgaga acgctaagac ctacatcgcc agccagggtc gtctggaggc cacggccaat 1260
gacttctggc agatggcgtg gcaggagaac agccgtgtca tcgtcatgac cacccgagag 1320
gtggagaaag gccggaacaa atgcgtccca tactggcccg aggtgggcat gcagcgtgct 1380
tatgggccct actctgtgac caactgcggg gagcatgaca caaccgaata caaactccgt 1440
accttacagg tctccccgct ggacaatgga gacctgattc gggagatctg gcattaccag 1500
tacctgagct ggcccgacca tgggggtccc agtgagcctg ggggtgtcct cagcttcctg 1560
gaccagatca accagcggca ggaaagtctg cctcacgcag ggcccatcat cgtgcactgc 1620
agcgccggca tcggccgcac aggcaccatc attgtcatcg acatgctcat ggagaacatc 1680
tccaccaagg gcctggactg tgacattgac atccagaaga ccatccagat ggtgcgggag 1740
cagcgtcctg gcctgggtgca gacggaggcg cagtacaagt tcatctacgt ggccatcgcc 1800
cagttcattg aaaccactaa gaagaagctg gaggtcctgc agtcgcagaa gggccaggag 1860
tcggagtacg ggaacatcac ctatccccc gccatgaaga atgcccatgc caaggcctcc 1920
cgcacctcgt ccaaacacaa ggaggatgtg tatgagaacc tgcacactaa gaacaagagg 1980
gaggagaaag tgaagaagca gcggtcagca gacaaggaga agagcaaggg ttcctcaag 2040
aggaagttag cgggtgctgtc ctcaggtggc catgcctcag ccctgaccct gtggaagcat 2100
ttcgcgatgg acagactcac aacctgaacc taggagtgcc ccattctttt gtaattttaa 2160
tggtgcacac cccccacct ctccctgacc ctgtatatag cccagccagg cccaggcag 2220
ggccaacctc tctcctcttg taaataaagc cctgggatca ctgaaaaaaaa aaaaaaa 2277

```

<210> 61

<211> 597

<212> PRT

<213> Homo sapiens

<400> 61

```

Met Leu Ser Arg Gly Trp Phe His Arg Asp Leu Ser Gly Leu Asp Ala
 1           5           10           15
Glu Thr Leu Leu Lys Gly Arg Gly Val His Gly Ser Phe Leu Ala Arg
          20           25           30
Pro Ser Arg Lys Asn Gln Gly Asp Phe Ser Leu Ser Val Arg Val Gly
          35           40           45
Asp Gln Val Thr His Ile Arg Ile Gln Asn Ser Gly Asp Phe Tyr Asp
          50           55           60
Leu Tyr Gly Gly Glu Lys Phe Ala Thr Leu Thr Glu Leu Val Glu Tyr
65           70           75           80
Tyr Thr Gln Gln Gln Gly Val Leu Gln Asp Arg Asp Gly Thr Ile Ile
          85           90           95
His Leu Lys Tyr Pro Leu Asn Cys Ser Asp Pro Thr Ser Glu Arg Trp
          100          105          110
Tyr His Gly His Met Ser Gly Gly Gln Ala Glu Thr Leu Leu Gln Ala
          115          120          125
Lys Gly Glu Pro Trp Thr Phe Leu Val Arg Glu Ser Leu Ser Gln Pro
          130          135          140

```

Gly Asp Phe Val Leu Ser Val Leu Ser Asp Gln Pro Lys Ala Gly Pro
 145 150 155 160
 Gly Ser Pro Leu Arg Val Thr His Ile Lys Val Met Cys Glu Gly Gly
 165 170 175
 Arg Tyr Thr Val Gly Gly Leu Glu Thr Phe Asp Ser Leu Thr Asp Leu
 180 185 190
 Val Glu His Phe Lys Lys Thr Gly Ile Glu Glu Ala Ser Gly Ala Phe
 195 200 205
 Val Tyr Leu Arg Gln Pro Tyr Tyr Ala Thr Arg Val Asn Ala Ala Asp
 210 215 220
 Ile Glu Asn Arg Val Leu Glu Leu Asn Lys Lys Gln Glu Ser Glu Asp
 225 230 235 240
 Thr Ala Lys Ala Gly Phe Trp Glu Glu Phe Glu Ser Leu Gln Lys Gln
 245 250 255
 Glu Val Lys Asn Leu His Gln Arg Leu Glu Gly Gln Arg Pro Glu Asn
 260 265 270
 Lys Gly Lys Asn Arg Tyr Lys Asn Ile Leu Pro Phe Asp His Ser Arg
 275 280 285
 Val Ile Leu Gln Gly Arg Asp Ser Asn Ile Pro Gly Ser Asp Tyr Ile
 290 295 300
 Asn Ala Asn Tyr Ile Lys Asn Gln Leu Leu Gly Pro Asp Glu Asn Ala
 305 310 315 320
 Lys Thr Tyr Ile Ala Ser Gln Gly Cys Leu Glu Ala Thr Val Asn Asp
 325 330 335
 Phe Trp Gln Met Ala Trp Gln Glu Asn Ser Arg Val Ile Val Met Thr
 340 345 350
 Thr Arg Glu Val Glu Lys Gly Arg Asn Lys Cys Val Pro Tyr Trp Pro
 355 360 365
 Glu Val Gly Met Gln Arg Ala Tyr Gly Pro Tyr Ser Val Thr Asn Cys
 370 375 380
 Gly Glu His Asp Thr Thr Glu Tyr Lys Leu Arg Thr Leu Gln Val Ser
 385 390 395 400
 Pro Leu Asp Asn Gly Asp Leu Ile Arg Glu Ile Trp His Tyr Gln Tyr
 405 410 415
 Leu Ser Trp Pro Asp His Gly Val Pro Ser Glu Pro Gly Gly Val Leu
 420 425 430
 Ser Phe Leu Asp Gln Ile Asn Gln Arg Gln Glu Ser Leu Pro His Ala
 435 440 445
 Gly Pro Ile Ile Val His Cys Ser Ala Gly Ile Gly Arg Thr Gly Thr
 450 455 460
 Ile Ile Val Ile Asp Met Leu Met Glu Asn Ile Ser Thr Lys Gly Leu
 465 470 475 480
 Asp Cys Asp Ile Asp Ile Gln Lys Thr Ile Gln Met Val Arg Ala Gln
 485 490 495
 Arg Ser Gly Met Val Gln Thr Glu Ala Gln Tyr Lys Phe Ile Tyr Val
 500 505 510
 Ala Ile Ala Gln Phe Ile Glu Thr Thr Lys Lys Lys Leu Glu Val Leu
 515 520 525
 Gln Ser Gln Lys Gly Gln Glu Ser Glu Tyr Gly Asn Ile Thr Tyr Pro
 530 535 540
 Pro Ala Met Lys Asn Ala His Ala Lys Ala Ser Arg Thr Ser Ser Lys
 545 550 555 560
 His Lys Glu Asp Val Tyr Glu Asn Leu His Thr Lys Asn Lys Arg Glu
 565 570 575
 Glu Lys Val Lys Lys Gln Arg Ser Ala Asp Lys Glu Lys Ser Lys Gly
 580 585 590
 Ser Leu Lys Arg Lys
 595

<210> 62
 <211> 2145
 <212> DNA
 <213> Homo sapiens

<400> 62

```

cggcagaact gggaccaccg ggggtggtga ggcggcccgg cactgggagc tgcactctgag 60
gcttagtccc tgagctctct gcctgccag actagctgca cctcctcatt cctgcgccc 120
ccttcctctc cggaagcccc caggatggtg aggtggtttc accgagacct cagtgggctg 180
gatgcagaga cctgctcaa gggccgaggt gtccacggta gcttcctggc tcggcccagt 240
cgcaagaacc aggttgactt ctgctctctc gtcagggtgg gggatcagggt gacccatatt 300
cggatccaga actcagggga tttctatgac ctgtatggag gggagaagtt tgcgactctg 360
acagagctgg tggagtacta cactcagcag cagggtgtgg tgcaggaccg cgacggcacc 420
atcatccacc tcaagtaccc gctgaactgc tccgatccca ctagtgagag gtggtaccat 480
ggccacatgt ctggcgggca ggcagagacg ctgctgcagg ccaagggcga gccctggacg 540
tttcttgtgc gtgagagcct cagccagcct ggagcttcg tgctttctgt gctcagtgc 600
cagcccaagg ctggcccagg ctccccgctc agggtcaccc acatcaaggt catgtgcgag 660
ggtggacgct acacagtggg tggtttggag accttcgaca gcctcacgga cctggtggag 720
catttcaaga agacggggat tgaggaggcc tcaggcgctt ttgtctacct gcggcagccg 780
tactatgcca cgagggtgaa tgcggctgac attgagaacc gagtgttggg actgaacaag 840
aagcaggagt ccgaggatac agccaaggct ggcttctggg aggagtttga gagtgttcag 900
aagcaggagg tgaagaactt gcaccagcgt ctggaagggc aacggccaga gaacaagggc 960
aagaaccgct acaagaacat tctccccctt gaccacagcc gagtgatcct gcagggacgg 1020
gacagtaaca tccccgggtc cgactacatc aatgccact acatcaagaa ccagctgcta 1080
ggccctgatg agaacgctaa gacctacatc gccagccagg gctgtctgga ggccacggtc 1140
aatgacttct ggcagatggc gtggcaggag aacagccgtg tcatcgatc gaccacccga 1200
gaggtggaga aaggccggaa caaatgcgtc ccatactggc ccgaggtggg catgcagcgt 1260
gcttatgggc cctactctgt gaccaactgc ggggagcatg acacaaccga atacaaactc 1320
cgtaccttac aggtctcccc gctggacaat ggagacctga ttcgggagat ctggcattac 1380
cagtacctga gctggcccga ccatggggtc ccagtgagc ctgggggtgt cctcagcttc 1440
ctggaccaga tcaaccagcg gcaggaaagt ctgcctcacg cagggcccat catcgtgcac 1500
tgcagcgccg gcatcgcccg cacaggcacc atcattgtca tcgacatgct catggagaac 1560
atctccacca agggcctgga ctgtgacatt gacatccaga agaccatcca gatggtgcgg 1620
gcgcagcgct cgggcatggt gcagacggag gcgcagtaca agttcatcta cgtggccatc 1680
gcccagttca ttgaaaccac taagaagaag ctggaggtcc tgcagtcgca gaagggccag 1740
gagtcggagt acgggaacat cacctatccc ccagccatga agaatgccc tgccaaggcc 1800
tcccgcacct cgtccaaaca caaggaggat gtgtatgaga acctgcacac taagaacaag 1860
agggaggaga aagtgaagaa gcagcgggtc gcagacaagg agaagagcaa gggttccctc 1920
aagaggaagt gagcgggtgt gtctcagggt ggccatgcct cagccctgac cctgtggaag 1980
catttcgcga tggacagact cacaacctga acctaggagt gccccattct tttgtaattt 2040
aaatggctgc atcccccca cctctcctg accctgtata tagcccagcc aggccccagg 2100
cagggccaac ccttctctc ttgtaaataa agccttgga tcaact 2145

```

<210> 63
 <211> 595
 <212> PRT
 <213> Homo sapiens

<400> 63

```

Met Val Arg Trp Phe His Arg Asp Leu Ser Gly Leu Asp Ala Glu Thr
 1             5             10             15
Leu Leu Lys Gly Arg Gly Val His Gly Ser Phe Leu Ala Arg Pro Ser
 20             25             30
Arg Lys Asn Gln Gly Asp Phe Ser Leu Ser Val Arg Val Gly Asp Gln
 35             40             45
Val Thr His Ile Arg Ile Gln Asn Ser Gly Asp Phe Tyr Asp Leu Tyr

```

50 55 60
 Gly Gly Glu Lys Phe Ala Thr Leu Thr Glu Leu Val Glu Tyr Tyr Thr
 65 70 75 80
 Gln Gln Gln Gly Val Val Gln Asp Arg Asp Gly Thr Ile Ile His Leu
 85 90 95
 Lys Tyr Pro Leu Asn Cys Ser Asp Pro Thr Ser Glu Arg Trp Tyr His
 100 105 110
 Gly His Met Ser Gly Gly Gln Ala Glu Thr Leu Leu Gln Ala Lys Gly
 115 120 125
 Glu Pro Trp Thr Phe Leu Val Arg Glu Ser Leu Ser Gln Pro Gly Asp
 130 135 140
 Phe Val Leu Ser Val Leu Ser Asp Gln Pro Lys Ala Gly Pro Gly Ser
 145 150 155 160
 Pro Leu Arg Val Thr His Ile Lys Val Met Cys Glu Gly Gly Arg Tyr
 165 170 175
 Thr Val Gly Gly Leu Glu Thr Phe Asp Ser Leu Thr Asp Leu Val Glu
 180 185 190
 His Phe Lys Lys Thr Gly Ile Glu Glu Ala Ser Gly Ala Phe Val Tyr
 195 200 205
 Leu Arg Gln Pro Tyr Tyr Ala Thr Arg Val Asn Ala Ala Asp Ile Glu
 210 215 220
 Asn Arg Val Leu Glu Leu Asn Lys Lys Gln Glu Ser Glu Asp Thr Ala
 225 230 235 240
 Lys Ala Gly Phe Trp Glu Glu Phe Glu Ser Leu Gln Lys Gln Glu Val
 245 250 255
 Lys Asn Leu His Gln Arg Leu Glu Gly Gln Arg Pro Glu Asn Lys Gly
 260 265 270
 Lys Asn Arg Tyr Lys Asn Ile Leu Pro Phe Asp His Ser Arg Val Ile
 275 280 285
 Leu Gln Gly Arg Asp Ser Asn Ile Pro Gly Ser Asp Tyr Ile Asn Ala
 290 295 300
 Asn Tyr Ile Lys Asn Gln Leu Leu Gly Pro Asp Glu Asn Ala Lys Thr
 305 310 315 320
 Tyr Ile Ala Ser Gln Gly Cys Leu Glu Ala Thr Val Asn Asp Phe Trp
 325 330 335
 Gln Met Ala Trp Gln Glu Asn Ser Arg Val Ile Val Met Thr Thr Arg
 340 345 350
 Glu Val Glu Lys Gly Arg Asn Lys Cys Val Pro Tyr Trp Pro Glu Val
 355 360 365
 Gly Met Gln Arg Ala Tyr Gly Pro Tyr Ser Val Thr Asn Cys Gly Glu
 370 375 380
 His Asp Thr Thr Glu Tyr Lys Leu Arg Thr Leu Gln Val Ser Pro Leu
 385 390 395 400
 Asp Asn Gly Asp Leu Ile Arg Glu Ile Trp His Tyr Gln Tyr Leu Ser
 405 410 415
 Trp Pro Asp His Gly Val Pro Ser Glu Pro Gly Gly Val Leu Ser Phe
 420 425 430
 Leu Asp Gln Ile Asn Gln Arg Gln Glu Ser Leu Pro His Ala Gly Pro
 435 440 445
 Ile Ile Val His Cys Ser Ala Gly Ile Gly Arg Thr Gly Thr Ile Ile
 450 455 460
 Val Ile Asp Met Leu Met Glu Asn Ile Ser Thr Lys Gly Leu Asp Cys
 465 470 475 480
 Asp Ile Asp Ile Gln Lys Thr Ile Gln Met Val Arg Ala Gln Arg Ser
 485 490 495
 Gly Met Val Gln Thr Glu Ala Gln Tyr Lys Phe Ile Tyr Val Ala Ile
 500 505 510
 Ala Gln Phe Ile Glu Thr Thr Lys Lys Lys Leu Glu Val Leu Gln Ser

515					520					525					
Gln	Lys	Gly	Gln	Glu	Ser	Glu	Tyr	Gly	Asn	Ile	Thr	Tyr	Pro	Pro	Ala
530					535					540					
Met	Lys	Asn	Ala	His	Ala	Lys	Ala	Ser	Arg	Thr	Ser	Ser	Lys	His	Lys
545					550					555					
Glu	Asp	Val	Tyr	Glu	Asn	Leu	His	Thr	Lys	Asn	Lys	Arg	Glu	Glu	Lys
565					570					575					
Val	Lys	Lys	Gln	Arg	Ser	Ala	Asp	Lys	Glu	Lys	Ser	Lys	Gly	Ser	Leu
580					585					590					
Lys	Arg	Lys													
595															

<210> 64

<211> 2734

<212> DNA

<213> Mus musculus

<400> 64

```

cctccagcac gctgtgctcc tgcagcagca gtggcttctt ggtgctgcct tggccatgac 60
acatatttga catgccctcc cttaacctac tcacagactc ttgctctgcg gcatggacca 120
aagagaaatt ctgcagcaac tactgaaaga agcccagaaa aagaaactca acagtgagga 180
gtttgccagt gaatttctga agctgaaaag gcaatccacc aagtacaagg ccgacaaaat 240
ctatcctaca actgtggctc agaggcccaa gaatatcaag aaaaacagat acaaggatat 300
tttgccctat gatcacagcc tggtagagct gtctctgtta acttccgatg aggattccag 360
ttatatcaat gccagcttta ttaaggggtgt ctatggacc c aaggcttata ttgctaccca 420
gggtccttta tctacaactc tcttggaact ctggaggatg atttgggagt accgcatctt 480
ggtcattgtc atggcatgta tggagtttga aatgggaaag aaaaaatgtg agcgttattg 540
ggccgaacca ggagaaacgc agctgcaatt tggccctttt tctatatcct gtgaagctga 600
gaaaaagaaa tctgattata aaatcaggac tctgaaggcc aagttcaata atgaaactcg 660
aattatttac cagtttcatt ataagaattg gccagaccat gatgtgcctt catctataga 720
ccctattctt cagctcatct gggatatgcy ttgttacc aa gatgtgact gtgttcctat 780
atgcattcac tgcagtgcg gctgcggaag gacaggtgtc atttgtgctg ttgattatac 840
atggatgctg ctgaaagatg ggataattcc taagaacttc agtgttttta atttgattca 900
ggagatgcga acacagaggc cttcgctagt tcaaactcag gaacagtacg aactgggtcta 960
cagtgtctgt ttagagctgt ttaagaggca catggatgtt atctctgata atcaccttgg 1020
aagagagatt caagcacaat gctcaattcc tgaacaaagc ctacaggtag aagctgactc 1080
ttgtcctctg gatttaccaa aaaacgccat gagggatgtg aaaacgacaa accagcatag 1140
caaacaaggg gctgaagcgg agagcactgg agggctctcc cttggcctta ggacttctac 1200
gatgaatgcc gaggaagagt tggttttgca ctcggtctaa tcaagccctt cttttaactg 1260
tttagagcta aactgcgggt gtaacaacaa ggctgtcata accaggaacg ggcaggcaag 1320
ggcttctcca gtcgtgggag agccccttca gaagtatcaa agtctggatt ttggttccat 1380
gttgtttggg tegtgtccta gtgtctgtcc cataaacaca gcggacaggt atcacaattc 1440
aaaggggccc gtaaaacgga ccaaatacac tccctttgaa ctgattcagc agagaaaaac 1500
aaatgacttg gccgtgggag acgggttttc atgcctggaa tctcagctgc atgagcatta 1560
cagtctcagg gagctgcagg tgcaaagagt ggcccatgtt tcttcagaag agctgaatta 1620
ttcactgcct ggtgcctgtg atgcgtcgtg tgtgccccgg cacagccccg gcgctttgag 1680
agtgcattctg tacacatctt tagcggaaga tcttattttt tcatcatccc ctccgaatag 1740
tgctgattcg aagatgtctt ttgatctgcc tgagaaacag gatggagcca cttcccctgg 18
cgctctattg ccagcctctt ctacaacctc cttcttttat agcaaccac acgactccct 1860
agtgatgaac actctgacca gcttttcccc accgttaaac caagagacag ctgtagaagc 1920
tccttctcgg aggacagatg atgaaatccc ccgcccactc cctgaacgga caccgagtc 1980
ttttattgtg gttgaggaag ccggagagcc ctcaccacgt gttaccgaat ccttacctct 2040
ggtggttaaca tttggagcat caccagaatg cagtgggaca tctgaaatga agagccatga 2100
ctctgtaggg tttacaccaa gcaagaatgt gaaactccga agtcccaaat cagatcgaca 2160
tcaggatggg tctctccac ctctctctcc agaaagaact ctagagtcct tctttcttgc 2220
tgatgaggac tgtatacagg cccaagccgt gcaaacttct tctactagct atcctgaaac 2280
cacagagaac tccacatctt ctaaacaaac attgaggacc cctggaaaaa gtttcacaag 2340

```

```

gagtaagagt ttgaagattt ttcgaaatat gaaaaaaagt gtttgtaatt cttcctcacc 2400
aagcaagcct acagaacgtg ttcagccaaa aaattccagc tcctttctga attttggttt 2460
cggaaatcgt ttttcaaaac ccaaaggacc aaggaaccgc ccatcagctt ggaatatgta 2520
acgcacctct ggatttataa gaatatttgt taaaattgta cctgcagata aagctacttg 2580
aatactgcta taataataat atcagtaatg aggatatatt ttgtcaatag tcttgaaaag 2640
gaaagcaata tgtgacaaac ttccagcaaa cttgtatttt catattcctt atatttcact 2700
gggaactgcc aataaagttt gtacttcaaa aaaa                                2734

```

<210> 65

<211> 802

<212> PRT

<213> Mus musculus

<400> 65

```

Met Asp Gln Arg Glu Ile Leu Gln Gln Leu Leu Lys Glu Ala Gln Lys
 1           5           10           15
Lys Lys Leu Asn Ser Glu Glu Phe Ala Ser Glu Phe Leu Lys Leu Lys
           20           25           30
Arg Gln Ser Thr Lys Tyr Lys Ala Asp Lys Ile Tyr Pro Thr Thr Val
           35           40           45
Ala Gln Arg Pro Lys Asn Ile Lys Lys Asn Arg Tyr Lys Asp Ile Leu
           50           55           60
Pro Tyr Asp His Ser Leu Val Glu Leu Ser Leu Leu Thr Ser Asp Glu
           65           70           75           80
Asp Ser Ser Tyr Ile Asn Ala Ser Phe Ile Lys Gly Val Tyr Gly Pro
           85           90           95
Lys Ala Tyr Ile Ala Thr Gln Gly Pro Leu Ser Thr Thr Leu Leu Asp
           100          105          110
Phe Trp Arg Met Ile Trp Glu Tyr Arg Ile Leu Val Ile Val Met Ala
           115          120          125
Cys Met Glu Phe Glu Met Gly Lys Lys Lys Cys Glu Arg Tyr Trp Ala
           130          135          140
Glu Pro Gly Glu Thr Gln Leu Gln Phe Gly Pro Phe Ser Ile Ser Cys
           145          150          155          160
Glu Ala Glu Lys Lys Lys Ser Asp Tyr Lys Ile Arg Thr Leu Lys Ala
           165          170          175
Lys Phe Asn Asn Glu Thr Arg Ile Ile Tyr Gln Phe His Tyr Lys Asn
           180          185          190
Trp Pro Asp His Asp Val Pro Ser Ser Ile Asp Pro Ile Leu Gln Leu
           195          200          205
Ile Trp Asp Met Arg Cys Tyr Gln Glu Asp Asp Cys Val Pro Ile Cys
           210          215          220
Ile His Cys Ser Ala Gly Cys Gly Arg Thr Gly Val Ile Cys Ala Val
           225          230          235          240
Asp Tyr Thr Trp Met Leu Leu Lys Asp Gly Ile Ile Pro Lys Asn Phe
           245          250          255
Ser Val Phe Asn Leu Ile Gln Glu Met Arg Thr Gln Arg Pro Ser Leu
           260          265          270
Val Gln Thr Gln Glu Gln Tyr Glu Leu Val Tyr Ser Ala Val Leu Glu
           275          280          285
Leu Phe Lys Arg His Met Asp Val Ile Ser Asp Asn His Leu Gly Arg
           290          295          300
Glu Ile Gln Ala Gln Cys Ser Ile Pro Glu Gln Ser Leu Thr Val Glu
           305          310          315          320
Ala Asp Ser Cys Pro Leu Asp Leu Pro Lys Asn Ala Met Arg Asp Val
           325          330          335
Lys Thr Thr Asn Gln His Ser Lys Gln Gly Ala Glu Ala Glu Ser Thr
           340          345          350

```

Gly Gly Ser Ser Leu Gly Leu Arg Thr Ser Thr Met Asn Ala Glu Glu
 355 360 365
 Glu Leu Val Leu His Ser Ala Lys Ser Ser Pro Ser Phe Asn Cys Leu
 370 375 380
 Glu Leu Asn Cys Gly Cys Asn Asn Lys Ala Val Ile Thr Arg Asn Gly
 385 390 395 400
 Gln Ala Arg Ala Ser Pro Val Val Gly Glu Pro Leu Gln Lys Tyr Gln
 405 410 415
 Ser Leu Asp Phe Gly Ser Met Leu Phe Gly Ser Cys Pro Ser Ala Leu
 420 425 430
 Pro Ile Asn Thr Ala Asp Arg Tyr His Asn Ser Lys Gly Pro Val Lys
 435 440 445
 Arg Thr Lys Ser Thr Pro Phe Glu Leu Ile Gln Gln Arg Lys Thr Asn
 450 455 460
 Asp Leu Ala Val Gly Asp Gly Phe Ser Cys Leu Glu Ser Gln Leu His
 465 470 475 480
 Glu His Tyr Ser Leu Arg Glu Leu Gln Val Gln Arg Val Ala His Val
 485 490 495
 Ser Ser Glu Glu Leu Asn Tyr Ser Leu Pro Gly Ala Cys Asp Ala Ser
 500 505 510
 Cys Val Pro Arg His Ser Pro Gly Ala Leu Arg Val His Leu Tyr Thr
 515 520 525
 Ser Leu Ala Glu Asp Pro Tyr Phe Ser Ser Ser Pro Pro Asn Ser Ala
 530 535 540
 Asp Ser Lys Met Ser Phe Asp Leu Pro Glu Lys Gln Asp Gly Ala Thr
 545 550 555 560
 Ser Pro Gly Ala Leu Leu Pro Ala Ser Ser Thr Thr Ser Phe Phe Tyr
 565 570 575
 Ser Asn Pro His Asp Ser Leu Val Met Asn Thr Leu Thr Ser Phe Ser
 580 585 590
 Pro Pro Leu Asn Gln Glu Thr Ala Val Glu Ala Pro Ser Arg Arg Thr
 595 600 605
 Asp Asp Glu Ile Pro Pro Pro Leu Pro Glu Arg Thr Pro Glu Ser Phe
 610 615 620
 Ile Val Val Glu Glu Ala Gly Glu Pro Ser Pro Arg Val Thr Glu Ser
 625 630 635 640
 Leu Pro Leu Val Val Thr Phe Gly Ala Ser Pro Glu Cys Ser Gly Thr
 645 650 655
 Ser Glu Met Lys Ser His Asp Ser Val Gly Phe Thr Pro Ser Lys Asn
 660 665 670
 Val Lys Leu Arg Ser Pro Lys Ser Asp Arg His Gln Asp Gly Ser Pro
 675 680 685
 Pro Pro Pro Leu Pro Glu Arg Thr Leu Glu Ser Phe Phe Leu Ala Asp
 690 695 700
 Glu Asp Cys Ile Gln Ala Gln Ala Val Gln Thr Ser Ser Thr Ser Tyr
 705 710 715 720
 Pro Glu Thr Thr Glu Asn Ser Thr Ser Ser Lys Gln Thr Leu Arg Thr
 725 730 735
 Pro Gly Lys Ser Phe Thr Arg Ser Lys Ser Leu Lys Ile Phe Arg Asn
 740 745 750
 Met Lys Lys Ser Val Cys Asn Ser Ser Ser Pro Ser Lys Pro Thr Glu
 755 760 765
 Arg Val Gln Pro Lys Asn Ser Ser Ser Phe Leu Asn Phe Gly Phe Gly
 770 775 780
 Asn Arg Phe Ser Lys Pro Lys Gly Pro Arg Asn Pro Pro Ser Ala Trp
 785 790 795 800
 Asn Met

<210> 66
 <211> 3717
 <212> DNA
 <213> Homo sapiens

<400> 66

```

gaacagcgaa gacagcgtga gcctggggccg ttgcctcgag gctctcgccc ggcttctctt 60
gccgacccgc cacgtttgtt tggatttaat cttcaggttg ccggcgcccc cccgcccgc 120
ggcctcgccg tgtgagaggg aagcaccctg gcctgtggct ggtggctggc gcctggaggg 180
tccgcacacc cgcccgcccg cgccgcttgc ccgcgccagc cgcgtccctg aaccgaggag 240
tcgtgtttgt gtttgacccg cgggcgcggg tggcgcgccg ccgaggccgg tgtcggcggg 300
gcggggcggt cgcggcggag gcagaggaag agggagcggg agctctgcga ggccggggcg 360
cgccatggaa ctgggcccgg agcccccgca ccgcccgcgc ctgctcttcg cctgcagccc 420
ccctcccgcg tcgcagcccc tcgtgaaggc gctatttggc gcttcagccg ccggggggact 480
gtcgctgtc accaacctga ccgtcactat ggaccagctg cagggtcttg gcagtgatta 540
tgagcaacca ctggagggtga agaacaacag taatctgcag agaatgggct cctccgagtc 600
aacagattca ggtttctgtc tagattctcc tgggccattg gacagtaaag aaaaccttga 660
aaatcctatg agaagaatac attccctacc tcagaagctg ttgggatgta gtccagctct 720
gaagaggagc cattctgatt ctcttgacca tgacatcttt cagctcatcg acccagatga 780
gaacaaggaa aatgaagcct ttgagttaa gaagccagta agacctgtat ctctgggctg 840
cctgcactct catggactcc aggagggtaa agatctcttc acacagaggc agaactctgc 900
cccagctcgg atgctttcct caaatgaaag agatagcagt gaaccaggga atttcattcc 960
tctttttaca cccagtcac ctgtgacagc cactttgtct gatgaggatg atggcttcgt 1020
ggaccttctc gatggagaga atctgaagaa tgaggaggag acccctcgt gcattggcaag 1080
cctctggaca gtcctctcg tcatgagaac tacaaacctt gacaaccgat gcaagctgtt 1140
tgactcccct tccctgtgta gctccagcac tcggtcagtg ttgaagagac cagaacgatc 1200
tcaagaggag tctccacctg gaagtacaaa gaggaggaag agcatgtctg gggccagccc 1260
caaagagtca actaatccag agaaggccca tgagactctt catcagtctt tatccctggc 1320
atcttcccc aaaggaacca ttgagaacat tttggacaat gacccaaggg accttatagg 1380
agacttctcc aagggttatc tctttcatac agttgctggg aaacatcagg atttaaaata 1440
catctctcca gaaattatgg catctgtttt gaatggcaag tttgccaacc tcattaaaga 1500
gtttgttata atcgactgtc gatacccata tgaatacgag ggaggccaca tcaaggggtg 1560
agtgaacttg cacatggaag aagagggtga agacttctta ttgaagaagc ccattgtacc 1620
tactgatggc aagcgtgtca ttgttgtgtt tccactgcag ttttcttctg agagagggtc 1680
ccgcatgtgc cggtatgtga gagagagaga tcgcctgggt aatgaatacc ccaaactcca 1740
ctacctgag ctgtatgtcc tgaagggggg atacaaggag ttctttatga aatgccagtc 1800
ttactgtgag cccctagct accggcccat gcaccagcag gactttaaag aagacctgaa 1860
gaagtccgc accaagagcc ggacctgggc aggggagaag agcaagaggg agatgtacag 1920
tcgtctgaag aagctctgag ggcggcagga ccagccagca gcagcccaag cttccctcca 1980
tcccccttta cctcttttgc tgcagagaaa cttaagcaaa ggggacagct gtgtgacatt 2040
tggagagggg gcctgggact tccatgcctt aaacctacct cccacactcc caaggttgga 2100
gccaggggca tcttgctggc tacgcctctt ctgtccctgt tagacgtcct ccgtccatat 2160
cagaactgtg ccacaatgca gttctgagca ccgtgtcaag ctgctctgag ccacagtggg 2220
atgaaccagc cggggcctta tcgggctcca gccatctcat gaggggagag gagacggagg 2280
ggagtagaga agttacacag aaatgctgct ggccaaatag caaagacaac ctgggaagga 2340
aaggctcttg tgggataatc catatgttta atttattcaa cttcatcaat cactttattt 2400
tatttttttt tctaactcct ggagacttat tttactgctt cattaggttg aaatactgcc 2460
attctaggtg gggttttatt atcccaggga ctacctgggc ttttaattta aaaaaaaaaa 2520
agaagtgggt aagaaaatgc aaacctgtta taagttatcg gacagaaagc taggtgctct 2580
gtcaccacca ggaggcgtcg tggtagtggg gctgctgcta ttttaagcaa gaactgaggt 2640
cctggtgaga gcgttgacc caggcttggc tgctgacat aagctaaatc tcccagacct 2700
accactggct accgatctct atttgggtgg aggttgggc ctgttcttcc taccaccagt 2760
tccatgacat tggctggtat aggagccaca gctaggaaag cacttgaggc agcatctgtt 2820
gggccacccc cggctcagtg ctggaatgtt gcagtgtagg tttccagggg aaggggggtg 2880
ggggtaggtg ggctccacag gatgggggag gagcatgtcc actgagtatc ttccttatgt 2940
tgctgtgata ttgatagctt ttattttcta atttttaaaa aatggtcata ttatgagtca 3000

```

```

aagagtatca aatcagtggt ggatggacca cccaaggggtg aggagagggg ctggaagccc 3060
tgggcattag gagaagggag tgggtgctgg catggacatg actggataga atttctcag 3120
gagggagcct ggtggatttt gaaggtaaaa ctttctgggt ttatcatgtt ttaattttag 3180
agacagggag tgatgaatca tcaccggttg tccccttatc taactccata aaagtgggaa 3240
tttcaaaaga acacctcatc caaggagctg gggcagactt cattgattct agagagacct 3300
gtttcagtcg ctactcatcc ctgccctctg gtgccagcct ccttaccatc acggcttcac 3360
tgaggtgtag gtgggttttt cttaaacagg agacagtctc tcccctctta cctcaacttc 3420
ttgggggtggg aatcagtgat actggagatg gctagtgtgt gtgttacggg tttgagttac 3480
atttggctat aaaacaatct tgttgggaaa aatgtggggg agaggacttc ttcctacacg 3540
cgcatcgaga cagattccaa ctgggtaaat atattgtttg taagaaagag attctgttgg 3600
ttgactgcct aaagagaaag gtgggatggc cttcagatta taccagctta gctagcatta 3660
ctaaccaact gttggaagct ctgaaaataa aagatcttga acccataaaaa aaaaaaa 3717

```

<210> 67

<211> 524

<212> PRT

<213> Homo sapiens

<400> 67

```

Met Glu Leu Gly Pro Glu Pro Pro His Arg Arg Arg Leu Leu Phe Ala
1      5      10      15
Cys Ser Pro Pro Pro Ala Ser Gln Pro Val Val Lys Ala Leu Phe Gly
20      25      30
Ala Ser Ala Ala Gly Gly Leu Ser Pro Val Thr Asn Leu Thr Val Thr
35      40      45
Met Asp Gln Leu Gln Gly Leu Gly Ser Asp Tyr Glu Gln Pro Leu Glu
50      55      60
Val Lys Asn Asn Ser Asn Leu Gln Arg Met Gly Ser Ser Glu Ser Thr
65      70      75      80
Asp Ser Gly Phe Cys Leu Asp Ser Pro Gly Pro Leu Asp Ser Lys Glu
85      90      95
Asn Leu Glu Asn Pro Met Arg Arg Ile His Ser Leu Pro Gln Lys Leu
100     105     110
Leu Gly Cys Ser Pro Ala Leu Lys Arg Ser His Ser Asp Ser Leu Asp
115     120     125
His Asp Ile Phe Gln Leu Ile Asp Pro Asp Glu Asn Lys Glu Asn Glu
130     135     140
Ala Phe Glu Phe Lys Lys Pro Val Arg Pro Val Ser Arg Gly Cys Leu
145     150     155     160
His Ser His Gly Leu Gln Glu Gly Lys Asp Leu Phe Thr Gln Arg Gln
165     170     175
Asn Ser Ala Pro Ala Arg Met Leu Ser Ser Asn Glu Arg Asp Ser Ser
180     185     190
Glu Pro Gly Asn Phe Ile Pro Leu Phe Thr Pro Gln Ser Pro Val Thr
195     200     205
Ala Thr Leu Ser Asp Glu Asp Asp Gly Phe Val Asp Leu Leu Asp Gly
210     215     220
Glu Asn Leu Lys Asn Glu Glu Thr Pro Ser Cys Met Ala Ser Leu
225     230     235     240
Trp Thr Ala Pro Leu Val Met Arg Thr Thr Asn Leu Asp Asn Arg Cys
245     250     255
Lys Leu Phe Asp Ser Pro Ser Leu Cys Ser Ser Ser Thr Arg Ser Val
260     265     270
Leu Lys Arg Pro Glu Arg Ser Gln Glu Glu Ser Pro Pro Gly Ser Thr
275     280     285
Lys Arg Arg Lys Ser Met Ser Gly Ala Ser Pro Lys Glu Ser Thr Asn
290     295     300
Pro Glu Lys Ala His Glu Thr Leu His Gln Ser Leu Ser Leu Ala Ser

```

305		310		315		320
Ser Pro Lys Gly Thr	Ile Glu Asn Ile Leu Asp Asn Asp Pro Arg Asp					
	325		330			335
Leu Ile Gly Asp Phe Ser Lys Gly Tyr Leu Phe His Thr Val Ala Gly						
	340		345			350
Lys His Gln Asp Leu Lys Tyr Ile Ser Pro Glu Ile Met Ala Ser Val						
	355		360			365
Leu Asn Gly Lys Phe Ala Asn Leu Ile Lys Glu Phe Val Ile Ile Asp						
	370		375			380
Cys Arg Tyr Pro Tyr Glu Tyr Glu Gly Gly His Ile Lys Gly Ala Val						
	385		390			395
Asn Leu His Met Glu Glu Glu Val Glu Asp Phe Leu Leu Lys Lys Pro						
	405		410			415
Ile Val Pro Thr Asp Gly Lys Arg Val Ile Val Val Phe His Cys Glu						
	420		425			430
Phe Ser Ser Glu Arg Gly Pro Arg Met Cys Arg Tyr Val Arg Glu Arg						
	435		440			445
Asp Arg Leu Gly Asn Glu Tyr Pro Lys Leu His Tyr Pro Glu Leu Tyr						
	450		455			460
Val Leu Lys Gly Gly Tyr Lys Glu Phe Phe Met Lys Cys Gln Ser Tyr						
	465		470			475
Cys Glu Pro Pro Ser Tyr Arg Pro Met His His Glu Asp Phe Lys Glu						
	485		490			495
Asp Leu Lys Lys Phe Arg Thr Lys Ser Arg Thr Trp Ala Gly Glu Lys						
	500		505			510
Ser Lys Arg Glu Met Tyr Ser Arg Leu Lys Lys Leu						
	515		520			

<210> 68

<211> 31868

<212> DNA

<213> Homo sapiens

<400> 68

```

ccagggtctg tgagccctcc agagttgggc cctggtggtc gaggccagtc ctgggggtca 60
ttgcattccc tccctcatta taaaatgggg cctggaggcc cggggcgga gaaaggggtc 120
cacaatactg cacggttaga ggccgagcca aggtggatc cggccagacc tccacaggtc 180
ttccttagcc tccacattgc ctacagtggt ggggcgccc gctgggggag aggtagcgga 240
ggcccaaagg gggccgaagc taactggacg gcagctcgcg atgggaacta cgcttcccag 300
catgcgacgg ggcaaagggg cctttcagcc gcgagcagcg cctcgaggt tctgctggga 360
gttttcattg acctctgtct cccctctcat tttgateccc gctcttctgc tctgggctcc 420
gcccccttct gagagccgat gacctggcag agtcccgcga gccgctttct tcttcccctc 480
tcattggccc agcctagctg ccattcggtt gagaggagga gaagttgctt actgattggt 540
ggattccggt tggcgccaac taggaaagg gggcggggca gcagctggcc cactgagcc 600
gctattaccg cgaaaggccg gcctggctgc gacagcctgg gtaagaggtg taggtcggct 660
tggttttctg ctaccgag gctgggcaagc ggggtgggaga acagcgaaga cagcgtgagc 720
ctgggcccgt gcctcgaggg tctcgcccgg cttctcttgc cgaccgcca cgtttggttg 780
gatttaatct tcaggttgcc ggcgcccggc cgcccgtgg cctcgcggtg tgagagggaa 840
gcacccgtgc ctgtggctgg tggctggcgc ctggagggtc cgcacacccg cccggccgag 900
ccgcttggcc gcggcagccg cgtccctgaa ccgcgaggtc gtgtttgtgt ttgacccgag 960
ggcgccggtg gcgcgcgcc gaggcgggtg tggcgggggc gggcggggtc cggcgaggag 1020
agaggaagag ggagcgggag ctctgcgagg cggggcgccg ccatggaact gggcccgag 1080
ccccgcacc gccgcgcgt gctcttcgcc tgcagcccc ctcccgcgtc gcagcccgtc 1140
gtgaaggcgc tatttggcgc ttacagcgcc gggggactgt cgctgtcac caacctgacc 1200
gtcactatgg accagctgca gggctctggc aggttaaggag agaccggcgg gcggtgctcc 1260
gggcccctgg cctcgggtgc ggccctcgag agatcaggcc aggaaacgga ccgggagtaag 1320
ggcgagaccc gtccgtccgg gttcgccgct cggggacagc cgggctaggg cctgccatgt 1380

```

gcacccccgc	ccggggcgga	tggtggggcg	gagaggccgt	cgggaccttc	caggggaaga	1440
ggtggagatc	cttgggccta	agcccagacc	aggcccacct	tcaccccttt	cggattgctc	1500
cgtactctcc	ttctatctct	atccctggaa	gctctttgga	atctaccccc	gcgggggaaa	1560
tcaggctctt	ctaggcactc	actttcacc	tttgctaaac	catcctcagg	atcttcggtt	1620
gctgtgatct	ttgttccttc	tcaacaaagg	accatggcat	tttctttcct	ggcggttatg	1680
taaaatcatc	tcagtccttc	gcctgtgca	cattcctgat	gtccactctg	ctgctttcct	1740
aaggccaggt	ctttttaccc	aactttcaga	aagcttcctg	ggcttttctt	gatagcaaaa	1800
aatgcacccc	acggtgtttc	ccgcggaaga	gctactttcc	cttcaatctc	tggcatcccg	1860
tttgctaagc	acatgtcttg	tgcgtttccc	aacttctgaa	aagcagaaag	tgtcctgttc	1920
aactttcatc	ccgactctgt	ctcagtactt	agaacacatg	cttttatttt	aggaaatacc	1980
ccaacatttg	ccatagccat	cataacctgc	aatgtgggtc	aaggccatgc	ccaccactc	2040
cttttttctc	ctttgcccac	gtgctaattg	ggtgttcaga	gtggcaaagt	gggatctttg	2100
ccacttgtag	tgtggcctag	aaatggtttc	tggcagcctg	gctgcttctt	aatctcatgg	2160
cctatctcct	gcatgtgacc	ttttaattat	atcctataaa	tcattcatgg	tttatttctg	2220
ttggtttcag	tgattatgag	caaccactgg	aggtgaagaa	caacagtaat	ctgcagagaa	2280
tgggctcttc	cgagtcaaca	gattcaggta	tttaagtctg	ctgtgtgggg	agcaatactc	2340
tgaatttctt	gaaacatgcc	ttttcaccca	ggaggttagt	tttggtgaga	acttgaggaa	2400
gtcatggcat	tgggtgataa	actttttttt	tttttttttt	gagacagagt	ttcgctcttg	2460
tgcgccaggg	tggcatgcaa	tggcatgcat	tcagctcact	gtaacctcca	cctcccggtt	2520
tcaagtgatt	ctcctgcctc	agcctccga	gtagctggga	ttacaggcac	gcaccaccac	2580
acccggctaa	ttttgtattt	tttagtagag	acagggtttc	ttcatgttgg	tcagcctggt	2640
ctcgaattca	caacctcagg	tgatccgcct	tcctcggcct	cccaaagtgc	tgggattaca	2700
gcgtgagcca	ccgcgcccg	tgataaacat	tattgagaac	aatacaaagg	agcccttgtg	2760
gctgtttatg	aagaaaggaa	ataggtttca	aatgtctata	aggaggtggt	gtgtgcttgc	2820
ccttgaagga	tgggtagtaa	agtataattc	accataccac	tgtaagtggc	attcaggcaa	2880
tcttactggt	taaaatacag	gatcaaatga	ttggaagtac	agtgtcatga	aatcatttca	2940
gtgatgctgc	tatggaggaa	attgccagtg	catttcattc	ttcatgaatt	catattactg	3000
cagagtttat	ctgtatttgt	acagataaga	ccattgggtg	aaagatcctt	taggttaaag	3060
gaactgcaag	agcaagtctt	aaaatgtaat	gtaggcttct	gtatgtagaa	tgtaatttta	3120
tatagaactg	gggataggat	tatcacttgt	agcagtgtgg	tgagcaaggg	ctgtaacacc	3180
tcactttcca	taaggctgta	tagacacatg	agctatgggt	gggtgggtct	gcgtcatctg	3240
agctggcata	ttagtaatgc	tgaacagtgt	ctccttcacc	ctgctgcctt	ttgtgagatg	3300
gacaccttgg	tgtcattttg	ttaaaggcag	caagtgcctg	ccttgcatgt	catgaccagt	3360
agttgtattt	ttctttttca	ttttgagaca	aggtctcaac	tctgtcacc	aggcaacctc	3420
tgctctccag	atttagagaa	ttcttctgcc	tcagcttccc	tagtagctgg	aattacaggt	3480
gtgggtctca	aacttctgat	ctcaggtgat	ccaccacttt	cgacctccca	aagtgtctgag	3540
attacagggg	tgagctactg	cacctggcct	tttttttttt	ttttttttga	gacagggctt	3600
tgtctgtttt	tccaggtctc	aggctggtgt	acagtggtac	aatcaggggt	cactgtagct	3660
tcaactttcc	gagctcaagc	gaacctccca	ctccagcctc	cccaagtagc	tgggactaca	3720
gacacgtgcc	accacaccca	actaattttt	tttttaactt	tggtagagtc	aagtctcact	3780
atgttgcccc	aggcttgttt	tgaacttgtg	gcctcaagcc	atcagcctgc	ctcagcctcc	3840
caaagtattg	gaatcacagg	tgtgagccac	tgtgcctggg	cagtagttgt	atttttcaag	3900
cctcatatga	tttgacaagg	taaaacgttt	aaaaactatg	ccaagaaaat	ctggtacctc	3960
ttgtttctat	ggttggaact	cacagaaagt	tatctgggtc	acctctatct	gaataaccaa	4020
acaatcatga	tatgaatcag	ttttattcac	cctcttctca	aatcctattt	cccttgatgt	4080
tatttgcaaa	taggagaaaa	aacagtaaat	acgctatgaa	aatattaaga	cttgtacaaa	4140
catgacattt	ttgacaatct	aatagacgta	acatcaattc	tggcaaaaagt	acaagccatg	4200
aatatttggt	gctgacttta	aataaagacc	caggtaacttt	gttttagtgtt	ttaattttaa	4260
tgacaaaatg	gtgttttttg	tattatttct	tgagagggtt	tttttttccc	catagggttt	4320
tgtctagatt	ctcctgggcc	attggacagt	aaagaaaagt	atgtattcac	tgttttcaaa	4380
tgtttatatg	tagaaaaaac	gtgtctaaac	ttaaatacct	tattttaaag	aagttcttca	4440
tacactggac	tggagccctg	gatttacctg	tgcttagaaa	cactctggaa	tctcaagaat	4500
gaatagtttg	tgtcagcaat	tttcagaact	ttttctcctt	tatttttagct	ataatttttg	4560
tgttctgttt	gggtcttacc	caaaccctta	ctctgtgctc	tgacatcata	gccttacaag	4620
aacatgtggg	gtttttttgt	ttgtttgttt	gtttgtttct	gaggcagagt	ctcactctgc	4680
cgcccaggct	agagtgcagt	ggctcactgc	aacctccacc	tcccagggtt	aactgattct	4740
cctgcctcag	cctcccgagt	agctgggact	acaggagtgc	accaccacac	ccggttaatt	4800
tttgatattt	tagtagacac	gaggtttcat	cgtgttggcc	aggccaggag	ttcgagactc	4860

ctgagactcc	tgacctcg	atataccctc	ctcggcctcc	catagtgc	atagtgc	4920
gattacatgt	gtgagccacc	gcgcccagcc	gaatgtgtgt	attttaagaa	aagacatggg	4980
tttgtttttt	ttcacctaga	agtctagtgt	tgggggtgct	cctgagaaca	ggacagcttc	5040
agaaatztat	tctcccatct	cttgccataa	atgggagtct	gtgactgtac	ccccaaagta	5100
caggctaaac	actatctctc	tgctaataatg	aatacctctt	tacttgtttt	attctcatta	5160
tttaccttct	gatctcatta	cagccttgaa	aatcctatga	gaagaatata	ttccctacct	5220
gtaagttagt	tccttgttta	ttttgagcta	atacctgtta	tctgttcctt	agctaccagc	5280
atgaccttga	taggagactt	aatttagaga	gtaaaaactg	cttttcttta	gtctcttttg	5340
agacaaggtc	ttgctctgtc	acccaggctg	gagtgcagtg	gcaaaatctt	ggctcactgc	5400
aacctctgct	tccttggtct	aagtgatcct	cccacctcaa	cttcagagg	agctgggact	5460
atatataggt	gcacaccatc	acaccggct	gatttttgta	ttttttgtag	acatgggggt	5520
ctcactctgt	tgcccaggct	ggtttcaaac	tcctgcctcg	gcctcccaaa	gtgctaggat	5580
tataggcaag	agccactatt	cccagccttt	ccttagtctc	ataagtactc	aagatgttcg	5640
gtctggagga	atttgcctc	catctctaac	agagctttat	taaaccagga	agggttcttt	5700
tgatgcaaat	gttatttggg	gattgatttg	gcactgtaat	ccctgttgag	gggggactg	5760
tagaccttgt	gagggttagt	gtaaacccat	ggaatggaaa	cttctatgct	gtgtcctggc	5820
tgtgtcctgg	caagggtgat	tcctggccac	atttactggg	tacctactgc	agtgtgtgag	5880
gagctagtct	accccttatt	caacccccct	tttttctctt	ttgagaactg	aattttccac	5940
tgaaatttta	tttgtgtgcc	ttaattattt	tcctttttta	ctttgatagc	agaagctgtt	6000
gggatgtagt	ccagctctga	agaggagcca	ttctgattct	cttgaccatg	acatctttca	6060
gtcatcgcac	ccagatgaga	acaaggaaaa	tgtgagtgtg	acttcaatgt	actaacctga	6120
ggcagagggtg	aaaccacag	gctgtcagtg	gcttagaagt	ggctgggctg	ctttctggga	6180
gactaaactt	ggccattatg	tgcggtcttt	ggagtcagag	aattctgggt	ttggatcctg	6240
cttactagct	gtgtgatgtt	ggcaaattct	tctcttttta	atctttgctc	ttttgtaaaa	6300
taggagtagt	aatacctttt	agggatgttg	tggcaataag	taagattatg	tatgaagtat	6360
tgaaaatggt	gcctgacagg	cgggagttgc	tcagattgta	gtcacagga	gtaattacat	6420
gtacaaatag	tgtttgtctg	gaaggctctg	cccaggctgt	ccttgccctc	ttgctctgac	6480
cctgaaatga	attgtaagct	taggaaaagg	ctctttggca	gtatttgtaa	gaacggggtc	6540
aacaagttct	agggaaatctc	agagtaactg	aaatgggtggc	ttggaagggtg	aatttctggg	6600
tatctaccct	gaatgagcct	ggcttttttg	ttctttttaga	cattgcacag	agtaggcata	6660
caaaacagtt	gtaatttttt	cagccttctc	tctactgtat	ttctatata	ttactttctc	6720
cccttttcca	ttcctgctga	aatgccacag	ttcataatcc	ttgtccttac	aatcttcagg	6780
tttagtgta	aaccactgc	ctccatgaac	tctcctgatg	atttctttat	caacctggga	6840
agtgtcatga	gaaagaatat	ggaaatgagt	tccagccttg	agtgccttga	acagtgtatc	6900
agcctctagt	gctttttacc	agggcaaagc	tgtactgatg	cctggttttc	ccccgaaata	6960
gcttctcagg	gttgcttgcc	tggagctttg	ttttaagggg	aaaacagcat	agatgggtgg	7020
taaaagagctc	tcactctgga	gttgctcctgt	ttacttcaa	tattttgggc	acattcctta	7080
acctgcaagg	tctagttttc	tcacctgtaa	aatcgggaca	atcagggtgt	atttgatggt	7140
taaaaagtta	atgcacagaa	agtacttagt	actgtgttgg	catagaaatc	actgtaatat	7200
tagccattac	tgcttttttt	ttttttttga	ttcttcatgg	ttttatttct	ctcagaactt	7260
taaaatgtga	acattctata	attcagccag	tctttacttc	caggtaactt	ctttattggg	7320
tcgcaatacc	cttttaaata	acatgctctt	gttcgggaag	gtagttagcc	gttcatcact	7380
ctttctgtct	aaataacatc	cagtgaacaa	tcccataggg	acaagaacat	gaaccagtg	7440
gtcccgcaca	atctgaagta	agttcaccat	gatagctgca	gcctcagtgc	cgaccgcgac	7500
cccagagacca	agggcaacgg	ggaactcagc	caccacgccc	agtgcctagc	attactgctt	7560
ttaatactta	attatgagtt	cttaagtga	tatttttaggg	caagggacct	gtgagtgttt	7620
tcattccata	aagtggaaatc	atacgatatg	tattctatca	tatctggctt	taaaaaacat	7680
tatgcttgta	agaatcgctc	acgttgagta	aaccagtagg	gctttttttt	ttttcattgc	7740
tttttagtata	gaatagaata	attataagta	gaaaaaatta	tctccagttg	gtaggaagag	7800
gtggaaaata	tgaagccctg	aaacagatgg	acctagatgg	aaaattttga	caactattca	7860
caggcaatta	tattagattt	tattttattt	tgcttttagat	ttcagaaagt	ttgtgattta	7920
gcttattcat	cgtgttttgt	atatttggca	gatacttgtg	ttaggaaata	cagtatgaca	7980
agaaaaagat	gttacttttag	aagttagctg	ttgacagagc	cttggaatt	cttagttacg	8040
cagatctatt	gttggaatta	ggtgaaactt	taatttggag	gcagaaaggt	gatcagtgc	8100
cactttcttg	cctctttcac	ccaagctgag	gcctgagttg	gttttcatgg	acagtatag	8160
tctcaactat	gtcttgcagg	aagcctttga	gtttaagaag	ccagtaagac	ctgtatctcg	8220
tggctgcctg	cactctcatg	gactccagga	gggtaaagat	ctcttcacac	agaggcgagaa	8280
ctctgccccca	gctcggatgg	tatgtgctct	ggctttcata	ggggaattcc	tgacaggaag	8340

aaaggattaa	aacaccttct	ttcatccaga	attgaaggca	ctacagtagc	actagctgtt	8400
tttaccttga	ctttgtcttt	tgaattaga	ctgtcaagca	ttcttgggtg	ttttgctgtg	8460
tctggagaac	agacaggcgg	tagtaagagt	gggagatggg	gtttgaaata	ttggagttgt	8520
gcaaggaata	atcgaccttg	ttaatctggg	aaatcctggg	tcatcctaaa	tgtatgtatg	8580
gtgggattat	atctcttctt	atcttcttct	tttttcttct	tttttcttct	aagggtcttc	8640
tggcaaaaac	cggaaagcct	gcgagacaaa	ttttaaaaga	gccgtaacac	tagatctctt	8700
acttaaaact	tgggtctttac	tatgcattct	aagtgtctct	caaggaactg	gagagagagc	8760
acttgacttc	ttccaaaggt	ggtttggtta	gaacagttat	gggccagggtg	ccatggctca	8820
tgcctataat	ctcagcactt	tggaaaactg	agacaggagg	atcgcttgag	tcctgggcag	8880
catagtgaga	ccacatctct	atcttcttct	tttttaattt	ttttaagaa	ctattatgga	8940
ttacagtga	tgtctaggct	gctgggcagt	tttggggctca	ctcgtttcag	ggctatgtat	9000
ttgccagaca	gggactgtca	ttacttccaa	agtttctctg	tgttgggtctg	aattggatta	9060
actgatagca	tctatagatt	ggagaggccc	aacttgagca	agatgaccac	atctggcttc	9120
caggtttacc	taggatctta	aatctgaaaa	tataccttct	caatctgctt	tgtgttctga	9180
ggttcagcca	gtattgttac	tctgtctatc	atttgcacaa	agcactttta	tatgttcttg	9240
tcttgtgaag	tggagttaat	ccacttgaac	agattaggaa	agtaccacta	gagaggtttg	9300
gatgatttac	caaaggatat	acataagtag	gaaaccagga	tttaatgac	tctggctggg	9360
tgtggtggct	catggctgta	atcccagcac	tttgggaggc	cgaggtggga	ggatcacatg	9420
aggtcaggag	ttcaagacag	cctgggtaac	atagttagac	cctatctgta	caaagttaaa	9480
aaataagctg	agtgtgggtg	cttgttctta	tagtcccaat	tagtcgggag	gctgaagtgg	9540
gaggattgct	tgagcccaag	aattcgaggc	tgcagtgaac	tatgatcaga	ccactgtact	9600
ccagcctgga	caatgaatcc	ctgtctcaat	aaacaatctc	taaattccca	agtacacagt	9660
aatgctttta	gagttgggta	tcagaaacaa	tatatctggg	gtgtgcttag	cgactagagc	9720
ctgtatcaca	tctgcaccta	ggaatcccag	aacatacctc	acaaatgttg	gtgtgatata	9780
gtgtgagctt	tcgtgataaa	ggtactgccc	cataataaag	ttatctaccc	ctaggctaaa	9840
aaaatttgcc	atctccagca	gtgtgcactt	ggggaggact	agagactgct	cagaacttgt	9900
tttatattgt	gaagcaaagc	taatgccaga	accagaatag	gccagctgca	gagaggattc	9960
cttgggtgcat	gatccactca	gaaaatcaga	gggccactta	actaacaaca	gattcatacc	10020
caaagagat	ttggatttta	aggattactt	gtaggtcata	acattgggac	taccctgcta	10080
ctgtgaaaaa	aataactcta	aacttttttt	tctggatttg	aaagtgccta	gaaaataaat	10140
aattcagtat	tagcagtgtt	tgtatttggt	ggatttatct	tcagggtgtg	atcttatgagc	10200
agtttttcta	aattttctat	attccatgtt	tagaggtttc	ccaaaaaaag	tatgactata	10260
ggttggctaa	tgaggtaccg	ccattttaat	tccaggaatg	gttttctctt	agggagatag	10320
tgtggtgaga	agagtttgga	ttttggagtc	aaacagatga	ggtgtataat	cttggtaacc	10380
tcttaagcac	cagtttctctg	atttgctaaa	taaaaggaa	aggattagct	accttttagtg	10440
tattgtgagg	cttctattgg	attatatgta	taaaagattat	atcgtagtat	ctggcacaca	10500
gtaattcctc	gtttaaaaac	tgagcattta	aatcccaagt	ctaaagaacg	aggatagatt	10560
ttatagaagg	aagttaccct	ttattccccc	ctgtcagaac	tggagttata	tataagtgca	10620
ttctctaggg	cattttatgg	tctttataga	gatttgcata	tgcttgccct	aactcatttc	10680
agcagattct	catactgtca	cagtcctcaa	tgctgatcgg	tgcttactga	tgcaaccttc	10740
taataaaaaga	aaccttggtc	ttcacaagag	gctatctcta	gtaccatta	taagggtgaat	10800
tgcttctggc	aagagttctc	tgtaaaggct	actgactact	cagggctgtg	tgtggtcctc	10860
aaatcattta	taatcttggg	atacattttc	atataatcag	taatggctaa	aattttgctt	10920
tgtataacaa	gtataacata	gtatgttttc	atcataaaaa	ctagtgacct	attcaaggaa	10980
atgaaagtgg	atcagagctc	tcattattaa	tccatgaatt	ttgtcttaca	gctttctctc	11040
aatgaaagag	atagcagtga	accagggaat	ttcattcctc	tttttacacc	ccagtcacct	11100
gtgacagcca	ctttgtctga	tgaggatgat	ggcttcgtgg	accttctcga	tggagagaat	11160
ctgaagggtac	cgtgtgtgtg	tgtgtgtgtt	cctatttgtt	ctactaatta	attacctctg	11220
gagaaggcat	gtgatgtgaa	aaagaacagc	aacagcagtt	ccccggggct	tgcttagctg	11280
atatttttgt	tcatttgggtg	ataattcatt	taataatagg	gctaccagcc	ttattaaatc	11340
cttttgattg	ggggatgggg	gcatcaaaaag	aagacacatg	atccttctta	ccctgaagga	11400
gctaactaac	aatctatatg	caagaaacat	gaaatcagaa	cggtatagga	tggtacatta	11460
aggatacttc	ctatccaggc	ctatctggtg	ttgttcaggg	agaaacacac	ctaaagcact	11520
taaacaatatg	ttagtctcta	caggctcttt	ttaaaatcag	tttttctgtt	cttttagaat	11580
gaggaggaga	ccccctcgtg	catggcaagc	ctctggacag	ctcctctcgt	catgagaact	11640
acaaaccttg	tgagttgttc	tagtgtgtct	ggagggaagcc	ctgcgtgatt	ggggcactgg	11700
acagagtagt	ccttagttga	gtatagccaa	agattgaaat	gcatgatagg	atctggggat	11760
ctgggtttta	ggcctcactt	tggctaccta	caaattatga	ccttttagtca	tgatatctct	11820

ctgcatgtct	cctgatgtat	aaggagtgtg	ggttaggagg	gaccatggtc	attcctagct	11880
tttaccatct	agtcagtttg	aaaaaagcct	atctgaagcc	tttagcctga	atactttact	11940
tttttttaggt	tattctcatt	tatattccac	agaacctagc	ataaaaattag	acaagcaaca	12000
gtaactcaca	ggattttttt	tgtttctgtg	ttttttgttt	ttttttttga	gacggagtct	12060
cgctcttggt	gcccattcta	gagtgcaagt	gcacaatctt	ggctcactgc	aacctctgcc	12120
ttccagggtc	aagtgattct	cctgcctcag	cctcccgagt	agctgggatt	acagggtgct	12180
gccaccacac	ccagctaate	tttgtatttt	cagtagagac	gggggttacat	tatgttggcc	12240
aggctagtct	cgatctcctg	acctcaggtg	atctgcccac	ctcgacctcc	caaagtgtcg	12300
ggattacagg	catgagccac	tgtgcctggc	tggatgtttt	ttgttgctgt	tttgtttgtt	12360
tgtttttgtt	tgtttttgtt	ttcattgaaa	atacctacct	gaggctgggt	attttcaggt	12420
agatattttc	gatttttaaaa	attatatata	atatatatatt	tatatatata	tatatatata	12480
tatactcaca	cacacacata	cacagtatag	atttgtgttt	ccatcagggg	tactttcaaa	12540
cagaaagcat	agtatatgta	gatacagaat	ctatagtgtg	tgtgtgtata	tatattcaaa	12600
atcacatata	tatacacaca	catacacatg	ctatagattc	gtgttttcat	catagggata	12660
ctttcaaagt	tagaagcaag	aatgtgccta	tacagatata	tacacctgta	tgttcagaga	12720
tatacacctt	taggtacaca	tctaaattga	taagttcata	ttttttaatt	ctcaataacc	12780
tgaactataa	ttacagaaca	aatgagctac	agtttttttg	tttgtttgtt	ttgttttgtt	12840
tttgagacag	agtctccctc	tgttgcccag	gctgggggtg	agtgcagtgg	tgtagtcttg	12900
acttgctgca	acctctgcct	cctgggttca	agtgcctctt	ctggctcagc	cttctgagta	12960
gctgggacta	caggcttacg	ccaccactcc	cggctaattt	ttttggtaatt	tttagtagag	13020
acgaggtttc	actatgttgg	ccaggtgtgt	ctcgaactct	tgacctcagg	tgatccatcc	13080
acctgcctcc	caaagtgtcg	ggattacagg	catgagccac	cgtgcccagc	caagctacag	13140
ttttgagatc	acttatggat	tatagtacat	tcattgtgat	agcttttgag	aaaatatgtt	13200
aacgcagtac	aaatgttatg	agtaaattta	ccaggtcatt	ttgataggca	taaaattaca	13260
taaaatgtga	gaacactttg	gaagtggctg	ttagttttat	agatttgatt	ttagagtcat	13320
aagcatgggc	ttgtaagctc	ttaatagtgg	ggaaatgtct	tccacaaatg	gttattacaa	13380
actaaccatt	gctgggagct	gtaatggaaa	ataaacttca	cacaaaagag	gaagaaaatc	13440
cccggctctc	atggggagcag	atgtgggagt	gatccattct	actggggact	atcaggaaga	13500
tttcaaagaa	gtgacattga	aatgttagca	tcaacttgaa	aatgaatggg	ttactgagat	13560
gtgaaaggac	attctgtgca	gaaggaaaag	ccaggccaag	acacatggag	tcgagaatag	13620
gctgagatgc	gtttagagag	ctgactcttg	ctaccactgg	tcagattggc	ttcccttggg	13680
ctctggaaaa	tttgtcttta	tttattttatt	tattttattga	gacagagtct	tgctctgtca	13740
cccaggctgg	agtgcagtgg	tgcaaatctt	agctcactgc	aaccaccacc	tcctgtgttc	13800
aagtgtattct	cgtgcctcag	cctcctgggt	agctgggatt	aaaggcacgc	accaccacac	13860
ctgggctaatt	tttttgtatt	tttaatatag	atgggggttc	ttcatgttgg	ccaggctgtt	13920
attgaaacttg	tgacctcaag	tgatcccaca	gtgttgggat	tacaggcgtg	agccaccgcg	13980
cccagcctgg	gaaattagtc	tttaaaagac	caagttagaa	aaaagacttt	gaacacaatt	14040
ttgaaaggca	tttgctactc	tgcccatccc	cactccctcc	aaatttacca	tcttaactat	14100
accttaacca	aagatgcccc	cattttttatt	ataacctggc	tactgtgcat	cttttctgga	14160
tttaagtggg	gtattttaaac	ccgttgacct	gcttaattaa	gcaagggtgca	agtaataaaa	14220
tggaggggaa	gataggcaag	ccaaaaatgt	gttcctgact	ggaagggtcac	acttctcttg	14280
acgcaggatt	atgtagacag	ttttttgtgag	ggcaaaggac	gtttttgctca	tctctatata	14340
atgtcagctg	agtatatatt	cattgagcac	taagtgtctca	gtgcctacta	tgtgccaggc	14400
cctgtgagag	ttgctaggac	tagatgaatc	ggcagtgtct	gttggctaatt	ttagaattga	14460
tcttagatca	ttccaggaaa	ccttcgggtt	atttgtctta	ccattcaagt	gaacagggtt	14520
taatgaaaga	tgggtctgtc	tgtttttttt	cctgtaagga	caaccgatgc	aagctgtttg	14580
actccccttc	cctgtgtagc	tccagcactc	ggtcagtgtt	gaagagacca	gaacgatctc	14640
aagaggagtc	tccacctgga	agtacaaaaga	ggagggaagag	catgtctggg	gccagcccca	14700
aagagtcaac	taatccagag	aaggcccatg	aggttagttt	cctagggttcc	tttttgctct	14760
agcacagata	ctgtattttt	cagttctaaa	aatctctact	tagtgggttca	tttattttct	14820
ttgctaagat	ttgctggggg	tttgtggggg	tgtgtgtgtg	tgtgggtgtg	tgtgtgtttc	14880
ttttaataga	gatgggatct	agcgatgttg	cccacgctgg	tcctgaactc	ctagcctcaa	14940
gtgatcctcc	tgccctggcc	tcccaaagca	ctgggattac	aagtgtgagc	caccacacct	15000
ggctgatact	tggctgtttt	catgttgggt	tttcatttgc	tttgagtatg	ttcataattg	15060
cctgttgaag	cattttttaag	atggctgctt	taaaatcttt	gtaagacaaa	tccaacatcc	15120
atccatagtg	ttgttggcat	ctgttgattg	tcttttctct	ttcaagttgg	gatttttctg	15180
gttcttggtg	tgaccgggtg	ttcttccatt	gtctcctgta	tattttgtgag	tctccggtct	15240
atgtaaattt	tacgttttag	caggcttctt	ctgatactgc	aagaaaggca	tgggtggaag	15300

tccgggttcc	ccagcacaaa	ctccattgac	accttgggtg	gggacttgtc	tcattattgc	15360
tgaggaggag	tggaagtcca	ttccatcccc	gtgggggtgt	gactggggca	ctgtatgaca	15420
gctgggcaaa	gggtggaggcc	cccgttgcct	gttggccata	attgtttctg	tggttgactag	15480
tagaatgatt	attgtctaaa	agtcttctgc	ctcaataggc	catcctttgc	ctagggagag	15540
caggcttttc	ttggggccttg	ttgtgttgcct	gtctccagct	tcattgagttg	aatgggttaac	15600
tcattcgttt	ttaattttct	tattttctgga	taaatctatt	tgaatctatg	aatttcccac	15660
tgcttttagat	ttgtctcata	acttttgacc	tgaaatgttt	ttattatcat	ttgttgtaga	15720
tattttatatt	ccttttaatc	cagacctatc	atggcctatt	aaatacttga	tttttataaa	15780
ggtctgtctt	tttttttttt	ttttttgaga	cgctctgtcg	cccaggctgg	agtgcagtgg	15840
cgcatctca	gctcactgca	agctctgcct	cccgggttca	tgccattctc	ctgcttcagc	15900
ctcccagtag	ctgggactac	aggaccccgc	caccacgcct	ggctaatttt	ttgtattttt	15960
agtagagacg	gggttttcaca	gtgttagcta	ggatgggtctc	catctcctga	ccttgtgac	16020
cgccgcctc	agcctcctaa	agtgtctgga	ttacaggcgt	gagccactgc	gcccagccct	16080
gtctgtctaa	ttcttcaagt	taattcattg	cattgtctcat	agttgtatag	gctgttttgt	16140
tgtttctgt	ttctgagaca	gggtctctct	gtcaccagg	ctggagtga	gtggcatgat	16200
ctccgctcac	tgactctctc	acctcccagg	ctcaagcagt	cctcccacct	caggctctca	16260
agcagctggg	actataggtg	tgtgccacca	aaccagcta	atttttgtat	tttttgtaga	16320
gacaggcttt	cgccatgttg	cgaggctgg	tctcaaactc	ctgggctcag	ggcaatcctc	16380
ccgccttggc	ctcccaaagt	gccaggatca	taggtgttag	acacagcacc	tggcattgggt	16440
gagctagtgt	catggttgtc	tgggcctaag	tcctatggtc	ccttgtgtta	tttttcttat	16500
ttattctgtg	gctagacaca	caaaacactg	gtttatttgt	atgtttttcc	ttcattatac	16560
tgctcttata	ttgaggtttg	gtattaagca	ttataaaatg	gtgaactacc	tgtgttttct	16620
gtggcatgaa	aaggtttaag	taaatctcat	cacagtctta	aaagggttaga	gagatgacag	16680
ctagggaaac	atttagcatt	taggcctact	gccttatcgt	atctgctttt	gtttttaatg	16740
ctttatgaat	gtttttaaag	tattgttcta	aaagaatatt	ttaataattg	catagtattt	16800
ttgttttggg	agagtgtgtt	ggttttgggt	tttgttcttt	ttgtttgtgg	ggggcacagg	16860
gtctagcgt	gtcactcagg	ctggagtga	ctagcacgat	cacagctcag	tacagcctcc	16920
atgggctcaa	gcactcctcc	cgcctcagcc	cccctagcag	ctgggactac	aggcatgcac	16980
caccatgccc	agttaattta	aaaaaaat	ttttttat	tttgtagaaa	agaggcttta	17040
ctgtgttgcc	caggctggcc	ttgaattcct	gggctcaagc	agtcctccca	cctcagcctc	17100
caaagtatct	gggactacag	gcacaggcca	gtgcacctgg	ccgatagtgt	tttgacttac	17160
aagtatacta	gaaataattg	aataaatcac	cctctggaca	tttagaattt	cccttcccct	17220
gattttcctt	ttatttctaa	ttaaaaatga	aattctgggt	tataagggca	agaacatttg	17280
tgaaacttta	cattgtatac	atgtcagaaa	atatctatca	atattttaata	atattctggc	17340
tgagtgtctg	ggttcactcc	tgtaatccca	gcactttggg	aggacaaggc	gggtggatca	17400
cgaggctcag	agttccatac	cagcctggcc	aatatggtga	aaccctgtct	ctactgaaaa	17460
tacaaaaaat	agctgggtgt	gggtggtatg	gcctgtaatc	ccagctgctc	aggaggctga	17520
ggcaggagaa	tcgcttgaac	ccgggaaatg	gagggtgcag	tgagcagaga	tcacgccact	17580
gcactccagc	ctgggtgata	gagtgtgatt	tcactcctaa	aaaaaaaaaa	aaagaatatt	17640
cattttcttt	ttctttcttt	ttgagacacg	ctggagtga	gtggcaggat	cctggctcac	17700
ggcaacctcc	gcctccccag	ttcaagcaag	tctctgctc	agcctcctga	gtagctggga	17760
ttacaggtgc	ccactgccac	gcctggctaa	tttttttgt	atttttagta	gaggcggagt	17820
ttcaccaagt	tggtccaggct	ggtcttgaac	tcctgacctc	aggtgatata	tccgccttgg	17880
cctcccaaag	tgctgggggt	acagggtgtg	gccactgtgc	ccggccagaa	tattcatttt	17940
cttttaccgt	aatagagatt	gaccttttta	tttccatatt	tgtaaaactt	tttttggata	18000
aaataaact	gttaataatt	attttgtata	tatattggcc	ctcatgtttt	ggttttat	18060
catatatatt	aatttttagt	attttaaatt	ccattgtgga	gaaaatgtca	agcattgcta	18120
gagtacagtt	atcatacctg	tgatattgtg	aaatatatat	ttagtcttct	tccccttctg	18180
tcataatact	cctaaaatct	ttggaatata	caaggctata	tctttttgta	tactaatgat	18240
tgatagcttc	aggggtgggac	tggtcactgg	aaagacagag	acatgattag	aggttggaac	18300
tttcagcccc	accctccaat	gtctacggaa	aggagagggg	ctaaaggctca	agttgatcac	18360
tcattggccaa	tggtttaatc	aatcatttct	atgtaatgaa	gcctccctaa	aaccttgaaa	18420
ggacaggggt	ccagagagctt	ctggatagct	gaacacatgg	aggttcctgg	aggttggggc	18480
acccaaggag	agcatggcag	ctccatgtcc	cttctcccat	acctcaccct	atgcatgtct	18540
tcttctatat	cctttgaata	tccttcataa	taaactggta	aatgtgtttt	cttgagttct	18600
gtgagccact	tctagcaaat	taaacccaaa	gaagggttca	tggaacccc	tacttaaagc	18660
tggtggctgt	agatcagaag	atccagaggc	ccaactgggt	tctgaagggt	gggtgtggtt	18720
tgaggactgg	gccctcaact	tcctgatctg	acgctctgca	ggtagatagt	gtcagaattg	18780

aattggacgg	caccagcta	ttttccactg	cagaactgct	tgcttgcttg	cttgcttgct	18840
ggtagggaga	aatccctca	tatctggggg	taacagcact	tctgtcttct	gttgctgttg	18900
agttagggaa	taagaaaaat	cactttgagt	ttgtgggggtg	ttttcctcac	acaaacatat	18960
catacagggc	taaatttctg	ggtgtttttt	tggttggttt	tttttttgag	accaagtctc	19020
gctctgtcgc	ccagactgga	gtgccatggg	tcatctctctg	ctcactgcaa	cctccgcctc	19080
tcaggttcca	gcaatttctc	cgctcagcc	tcccaagtag	ctgggactac	aggcgccac	19140
caccacgcct	ggctaatttt	ttatattttt	agtagagacg	gggtttcacc	atgttggtgaa	19200
ggctggtctc	gaaccctga	catcaagtga	tccactcacc	tccgcctccc	aaagtgtgtg	19260
gattacaggg	atgagccacc	acgcccggca	gagctaaatt	tcttactatc	aaatgtcaaa	19320
tatccagtct	gggttcagtt	ttccccagtt	gtctcctaag	tactttttaca	gtttatttgt	19380
taaaaatctg	atccaaataa	agtctataca	ctgtagtgtg	tcaataggtc	tcttactctt	19440
cagatttcag	tgctccatct	gtttccctct	tgcatatttt	tatttggtga	agagctcaag	19500
tcatttgtcc	tgcaaaaggt	cccacagtcc	tgtggggtct	tcagacattg	tcttctatcc	19560
cctatatattg	cttaacctaa	ctctggaaag	gatggattga	attccagttc	tatttggttg	19620
gcaagaatat	cacataggtg	attttgtcta	cttgatcag	gaagtataat	gtgccaggca	19680
gccattggtg	attgctgccc	agatttttta	cttcatttca	ccagggtttc	agaaagatga	19740
tactgcagtt	tttacattct	ttcctcatta	attagctaga	atatactctat	aaagagaaa	19800
ttacactcat	caaacactgt	ggttaccctt	gggaaaggca	ggatgaatat	tggatctctt	19860
tatttgccag	tttccaaata	atgccctacc	aagcatcttc	caaagtgtga	agcaagactt	19920
atagttgttt	ttcaataata	atcaggaatt	catgggttaa	aacatttaat	gtgtttctgt	19980
gtattacaag	tattatcctt	ttactcaa	tatcccttt	ttaacagctg	gcttctctt	20040
ctcattgaat	aaagctaaga	cgtaggccgg	gcgcggtggc	tcacacctgt	aatcccagca	20100
ctttgggagg	ccaaggcagg	cagatcacct	gaggccagga	gttcaagacc	atctggccaa	20160
catggtgaaa	ccccgtctct	actaaaaata	caaaaattag	ctgggcgtgg	tggcgcacac	20220
ctatagtctc	agctgctctg	gaggctgccc	cagaatcgct	tgaacctggg	aggcagaggt	20280
tacagtgagc	caagatcact	gtactccagc	ctgcactcca	ctcctgtact	ccactgcact	20340
ccagcctgag	cgacagagcg	agactctgtc	tttttaaaaa	aaaaaaaaaa	aaaaagttaa	20400
gacatacttt	ttctaaactt	aatcctagtt	ttaaccccc	ttgtttcttt	ctctttttct	20460
ggagatagtt	tcagctgtgc	accaggtctg	gagtgcagtg	gcaccatcac	cacttgctgt	20520
agcctcgacc	tccccaggct	caggtgatcc	tcccacttca	gcctcccaag	tagctgggac	20580
tacaggcaca	caccaccatg	cccagcttgt	gtgtgtgtgt	gtgtgtgtgt	gtgtgtgtgt	20640
gtgtgtgtgt	gtgtgtggac	aggtcttgtc	tcttgcattc	ggtctggaac	tcttgggctc	20700
aagcgattca	cctgccttgc	ccaggtctgt	ctggaactcc	tgggtcaag	tgagtaaccc	20760
accttggcct	cccaaagtgc	tgggattaca	ggcatgagcc	aaaccacctg	cacccccctt	20820
tttttttttt	ttttttaagg	aaggaaggaa	aacttagttt	cagagcaatt	cgggttagaca	20880
ctggaataat	aggagaccta	gtcaataacc	cacatctgtt	tttgttcact	ccagattcaa	20940
taaaaataaaa	taaaaacttc	ttactaaatg	taggcattaa	catttttagtc	tcctcgagac	21000
atgctccaag	tgaatgtttt	cagaagttcc	attcagaacc	cttgtctcat	tctctacctt	21060
tgatttggtta	cagactcttc	atcagctctt	atccctggca	tcttccccca	aaggaaccat	21120
tgagaacatt	ttggacaatg	acccaaggga	ccttatagga	gacttctcca	aggtaattgc	21180
aagcagagct	gctctggcaa	gtgtaggagg	gagtgtgggt	atttagaatc	ccactcagcc	21240
tgtctccctc	cccagggttg	ttcctggcat	acctccaaaa	ggacacagtt	aaaagaatgt	21300
taaaggtagg	gaagcaaaact	tagtttctca	tgatcaggta	tatgttggtt	tctgagactg	21360
tagatatcac	tatagctgat	gggcagtttt	aggtagggag	ctgtccacca	accaccttga	21420
ttgtaaccca	aagactaggc	tctctgggaa	ctgtgttatt	ataaaaaatag	taattagcag	21480
gatagtgtac	agcagaaata	aatctgtagc	cacactacaa	gtctgcatgt	tgaaagggtta	21540
tcttagaagg	tctgggattg	agactgaatt	tctccgttca	gagaagcttg	gccattgagg	21600
gaaaagaccc	tccaggaagt	ctagaggaag	atcttcta	agcctgatat	actacatgaa	21660
ggcttggctg	cagtaaaata	caaggctagg	acagggaatg	tgtcaatagc	agcttcttta	21720
atcacatttt	gacttgaagg	ttaccagatc	aatgttttat	tcattaattt	agttaacatt	21780
tattgaagca	cttatgtgtt	aggcagagat	tccaaaaatga	gatacagttc	cttccctcaa	21840
agaatttagc	atgtggttgg	agaggtgaga	cgtgaactac	atgtaccaca	tggtagactg	21900
aaataaattt	tagtgagggtg	taaacataaa	cagcatgccg	tgagaagtaa	aagggtttat	21960
cttggctagg	gggttgggga	acgtctgggg	ttgggcccgtt	gatattttcag	cccaaattggg	22020
ttttgaagga	acggagaatg	aagagaacaa	gcaaagatcc	agctgtatcc	tcagtttttg	22080
aaccttctct	tggttggcag	ggagagatgt	ggtcttacta	tggtgtctcag	gctgtagtgc	22140
agtggctatt	cgcacatgct	atcatagtag	actgtagcct	caaacttatg	gcctcaagtg	22200
ctccccctgc	ctcagcctcc	caagtagctg	ggactacagg	catgcaccac	cacactcagt	22260

ggaattttca acttgaattg aggcctgggt atatttgtct taatgggcct atgcatgggg 22320
 atagatgaac tcttgggtca gccagtcacc ctaatgagta attgctaatt tgtgcatctt 22380
 cctcctcaag gctgggctag gtctcttttt ttcctatccc cagtgcctgg caccatgctg 22440
 gacatagcag gtgctcagta aatgagtga atctgtatgt ttaagtgcta ttcgcagtct 22500
 aactactgac gtgtggattc ttgacaaaag caggaggaaa atgagattac ctgagggtttc 22560
 tttattttaa tctgccttac tagctaggta acctgggata aggtgctcaa aatggggata 22620
 atatacctca ttgggtttgt tgaaaattaa atgtcaggat gttaatgaag taactagaag 22680
 agtaactagt gtgtactaac taatgtttgt ttgcttgttt gtttgtttgt tttttgagag 22740
 ggagtcttgc tctgtcacc aggctggagt gcagtgggtc aatctcagct cactgcaacc 22800
 tccgcctcct gtgattcaag cgattttccc actccagcct tccgagtagc tgggactata 22860
 ggtgcatgct aacgcccggc taatttttgt atttttaaaa gagggtgggt ttcaccatgt 22920
 tggccaggct tgtctcgaac tcctgacctc aggtgatcca ctgacctcg cctcccaaag 22980
 tgctgggatt acagggtgtga gccaccgtgc ctggccatta atgtttgttt tttaaaagat 23040
 gcctcctacc agccagacaa aacagtataa gtgtgaataa tatataggct ttcagattct 23100
 ctaagtatct ttttttcttt ttaagggtta tctctttcat acagttgctg ggaaacatca 23160
 ggatttaaaa tacatctctc cagaaattgt aagtccatcc ttttgaaacc caccacacat 23220
 cgggtacttg aatctagttt tccctgacgg tcaaagttga ttctccctaa ttttctctca 23280
 acagatggca tctgttttga atggcaagtt tgccaacctc attaaagagt ttgttatcat 23340
 cgactgtcga taccatag aatacagagg aggccacatc aaggatgga ttctgagac 23400
 ttgctgtaga aggagcccta aacaggatct gtgggtttta agtggggagg acagtgcac 23460
 ctggccactt agctcatatg ctagtgtgta gaattttgaa acaatacagt gagtgtggaa 23520
 ggcatttgat tccgggtgct cttaacgaat gttcccttgt ctgcaatact ctctaccacc 23580
 ttgtgctaca gttattcttc atgtttgtcc ctacacccat cattatcaag gacacttgta 23640
 ggaggtaccc actgatgttt aagtcattcg ggggacaaga atgggtttca tagcatttaa 23700
 gaggcttggg taccaatgct tgagcaccct agggctcctg atgaggagaa gaccatctct 23760
 ggcaacatgt cctggtgtct gtgccaggct tagtgatgcc tccaaagttg attgttcagc 23820
 aagctgcctg gtggaggggc gtgttgggac acacgttccc aagaagaaag gaactgattt 23880
 tgccatttta atcttttttt tttttttttt tttagacag agtccgctct gtcgccaggc 23940
 tggagtgcag tggcatgac tcggatcacc acaacctctg cctcctgggt tcaagcaatt 24000
 ctctgcctc agccttccaa gtagctggga ctacaggtgc acgctgccac gcccggttaa 24060
 tttttttttt ttttttagtag agacgggggt tcacctgtt gcccggtctg gtctcaaact 24120
 cctgagctca ggcaaacgc ccgctcagc ctcccaaagt gtaggatta caggcatgag 24180
 ccacggcgcc tggcctgcca ttttaattgt ttacccgatt aatagtgttt aaatatagta 24240
 aggaggtact ttaaatacga tgttactgtt tgccattgtc ttgtggcttt tgaaaatccc 24300
 caaatttata aaactaccta taaagtgtac cattgtcata tttgaattgc ccatttccag 24360
 tccccatgtg cattactgta tgatgaacgt gtacggacct acaaagctcc attgagatac 24420
 aggtgccaaa tggctactg ggctattcag ctagaagaac tgcaaaaatc acaaactggt 24480
 ctgttgact taaagatcac tcttgatgaa tcattacatc ttgctgaatc attacttcat 24540
 gtgtgaaacg tgcaggttcc aagggtctct gttgtcttca cagggtgcag tgaacttgca 24600
 catggaagaa gaggttgaag acttcttatt gaagaagccc attgtacctc ctgatggcaa 24660
 gcgtgtcatt gttgtgtttc actgagagtt ttcttctgag agaggtcccc gcatgtgagt 24720
 gctgcacgga actgggttct ggggcacagg ctccatgatg cttttgtggg acatggtggt 24780
 ttgtggcttg cacttgagc atatttttagc atatcaagca acctctggca cataacaagc 24840
 cattttcata tgtaatttta tcttgagggt aactttggct ctccagctc ccccgactgt 24900
 ccttagtctg atctgtgggg ctactgttct catgtgacct ctttcaagta caaagtgacc 24960
 gttccttatg caaatgccag aaaagtgtga agttctcatt ctgtaaaacc tcatatgata 25020
 tgatgctttg aaacacttga tattattacc aatttcaggg tgaaaagaaa aaagggggcc 25080
 aaagagctgc ccatcagtca tctgtgtcca ttctaaaagg attgcaagcc tgctgtttgt 25140
 caggcactga caataaaaat gtaactacag taaaacacag tacagtaaaa ataccacagc 25200
 gagcaggacc aacaaggacc ctactgcagc agagatccaa gtggggatcc gtataaatgc 25260
 taggaggaca ggcagagagg taggacagag agtgcagctt aactaggatg gtccaaggga 25320
 gacttctgca ggaccacgtt cttatgccac ctttttattt tgaaccaatt tattttaaaa 25380
 aacattttta aattaaaaaa tttcaatttt ttttttttga cggagttttg ctcttgttgc 25440
 ccaggctgga gtgcagtggc acaatctctt ctactgcaa cctctgcctc ccaggttcaa 25500
 gcagtctctc tgccctagcc tcccagtag ctgggattac aggcagcgc catcacgcc 25560
 ggctaatttt gtatttttag tagaggcagg gtttctacat gttggtcagg ctggtcttga 25620
 actcccgacc ttaggtgatc cgctgcctc agcctcccaa agtagtggga ttacaggcgt 25680
 gagccactgc acctggcttt ttctttcttt ctttctttct tttttttttt tttttttgag 25740

gcagaggcac	actgtttttca	cccagactgg	aatgcagtgg	catgatctcg	gctcactgca	25800
acctccacct	cctgggttca	agcgattctc	ctgcctcagc	ctcctgagta	gctggggataa	25860
caggcgtgca	ccaccacacc	cggtcaattt	ttgtatttgt	agtagagatg	gggggtttcac	25920
catgttgccc	gggctggctc	tgaactcctg	acctcaggtg	atccacccgc	cttgacctcc	25980
caaagtgctg	ggattacagg	tgtgagccac	cacgcccagc	agaaatttca	aatttttgaga	26040
tggggctctta	atatattggc	caggttgggc	tcaaactcct	ggcctcaagc	aatcctctct	26100
ccttggcctc	caaagtgcga	ggattgcagg	catgagccac	tgtgcccacc	cctttgaacc	26160
tttttttttt	tttgagacgg	agtctcgcct	tgtcaccacg	gctggagtg	agtggcaca	26220
tctcgactta	ctgcaagctc	cgctcctcgg	gttcattgcca	ttctcctgcc	tcagcctccc	26280
gagtagctgg	gactacaggt	gcccaccatc	acgcctggct	aatttttttg	tatttttagt	26340
agagacaggg	tttcaccatt	ttagccagga	tggctctccat	ctcctgacct	tgcgatctgc	26400
ccgtctcggc	ctcccaaagt	gcttggatta	caggcgtgag	ccactgcgcc	tgacctgaac	26460
cattttaaag	ctcaagaaga	ggtgaggtta	tggctgggca	cagtggcacc	tgtaatccca	26520
acacttttggg	aggccgaggc	aggaggatca	cttgctcggg	agtttcagac	cagaccaacc	26580
tgggtaacac	agtgggacca	cacctctaca	aaaaatagga	ggtgggagga	tcgtttgagc	26640
ccagcaggtc	gaggctgtgg	tgagccatga	tcatgccact	gtactccagc	ctaggtgaca	26700
gagtgcgatt	ctgtctctct	ctcacacaca	cacacacaca	cacacaaagg	26760	
ttatacttgc	acacacttca	cctgatttta	tttaatttta	acattttgtc	acattttgat	26820
gtacatgctc	tacacacagg	caactacagt	acaacttgac	acttttgact	gtcatctcat	26880
aagtccttca	aacatctgtc	tccaaaggat	gctcattcat	gaatggaatt	attcactcag	26940
cagttttttt	gtttgtttgt	ttgagatgta	gtcttgcctc	gccaccagga	ctggagtgc	27000
gtggtgcgat	ctcggatcac	tgcaacctcc	acctcccggt	ttcaagcaat	tctcctgcct	27060
caggctccca	agtagctggg	actacgggtg	catgccacca	tgccaagcta	atgtttgtat	27120
tttttagtaga	gacgggggtt	tgctacattg	gccaggctgg	tctcgaactc	ctgacctcaa	27180
gtgatctacc	cgctcagacc	tcccaaagtg	ctgggattat	aggcctgaaa	caaactaatc	27240
tggacacaca	tacacacaca	tgtaaattgt	ttttaaaccc	acaaaagatg	ctgctctctt	27300
ttttttttat	ttttgagtca	gggtcagctc	ctgttgtcca	ggctggagta	cagtggcagg	27360
agcacagctc	actgtagcct	ctgcctccca	ggctcaagtg	attctcccac	ctcagcctcc	27420
caggaagcta	ggaccacaaa	catgcacac	catgcctggc	taatttttgt	attttttata	27480
gagacagggg	ctcactgtgt	tgcccaggct	ggtctcaaac	tcctgggctc	aggcaatcct	27540
ggcctcccaa	agtgccttga	ttacaggtgt	gagccgccat	gcccagccca	aaagatgcta	27600
ttctcttaat	ctctcatttc	cccatcttcc	tctttaacac	ctctaataata	aaggacatta	27660
ttataaccata	ttgaaacttc	acctagatat	acagaaaacg	ccccatctct	gtattctgta	27720
tttgcaagct	gcatgtttat	atcaccatct	acagataccc	cttacacttc	gttccccact	27780
tgagtttgcg	catcactggc	tttctgttgt	tccactgggg	aaagatttgg	gattcacagg	27840
tgaactcttt	tttttttttt	tttttttttt	tgagttggaa	tctcgccctt	tcgcccaggc	27900
tggaatgcag	tggcacaaac	tcggctcact	gcagcctcct	cctcccggtg	tcaagcattt	27960
ctctgcctca	gcctcccaag	tagctgggat	tacaggcacc	tgccaccacg	cccagcta	28020
ttttttagtagt	tttagtagac	acagggtttc	actatcttgg	ccaggctggg	ctcgaactcc	28080
tgacctcgtg	atccaccgcc	tcagcctccc	aaagtgcctg	aattacaggt	gtgagccacc	28140
gcgccagcc	aaactccttt	taaccacagg	caaagtgttt	aagctacgtg	ctgcagagga	28200
agctgctgcc	catcctcat	gagcagctaa	caaaggcccc	aaaccactga	gcttcaagag	28260
aaaatcagca	gatactcttg	gctcttgtgt	accagatacc	tttctagata	ctgagggaga	28320
agagcagtga	acaaaacaga	ccaaaaaatc	tctgccttca	tggaaacttac	atttcggagt	28380
ggacaggaga	tcgagaccag	cctggccaac	atggtgaaat	cccgctctcta	ctaaaaatac	28440
aaaaatttagc	caggcgtggg	ggcggacacc	tgtaatccca	gctacttttg	aggctgaggc	28500
aggagcatcc	cttgaaccac	ggaggcagag	gttgacagtga	gccgagatcg	cgccagtgc	28560
ctccagcctg	ggcgacagag	tgagactcca	tctcaaaaaa	aaaaaaaaaa	aggtgactgg	28620
gtgcggtggc	taactcctgt	aatcccaaca	ctttggggagg	ccaaggcagg	tggatcaca	28680
ggtcaagagg	tcgagaccat	cctggccaac	atggtgaagc	cccatctcta	ctaaacatac	28740
aaaaatcagc	tgggcggtgg	cacgcgcctg	tagtcccagc	tatttggggag	gctgaggcag	28800
gagaattgct	tgaaccgggg	agacggagat	tgaggtcac	gccccttgac	28860	
tccagcctgg	tgacagagtg	agattctgtc	tcagaaaaaa	gaaggtgctt	cagaggaaaa	28920
taaggccagt	ggtggagctc	ccaggcaggc	tggaggaaaca	gtagtggggc	tcgaggggct	28980
ggcgtggggg	gaacaagggg	cagagcagca	gtaggggcct	gtagagctgt	aggcctctga	29040
aggacttggg	gcctcgggct	ttttcaccac	gggcgaggca	gtaagcagcc	attggctgga	29100
tattgaagac	cattcagctc	aagtagagga	tagaaacagg	gccccaggcc	aggagcaagt	29160
tcagcctctt	taaaagccac	agaaagaaac	aagccactt	atgtagaagg	aggtgagtga	29220

```

gggagcctgg ctgaagagaa ggctgggggtg gagaaagcaa ggggaagctg gctcatatag 29280
tgaaaacttg ccacaaactg tgggtggtgaa ggtgctgggc aggactcaga tgctaggatt 29340
gttggagaaa ggaaaatttg ggaagagacc atctactggc actggctgtg agtgctgctc 29400
atgtggccag gaacttgcaa ctcagcactg attgtttcta agaataaatg tcaagttggg 29460
aagatgtgta taagggggac ttagaccaca actgctgctt tgactgctgt gccttgttgc 29520
tgtgctggaa aagctaaccc tgctttggcc ttccttcccc tgactagggt ccggtatgtg 29580
agagagagag atcgctggg taatgaatac cccaaactcc actaccctga gctgtatgtc 29640
ctgaaggggg gatacaagga gttctttatg aaatgccagg taagactggg gttgtggaga 29700
gcatctctcc tcccctgccc ccagtggtag actaatggat ctgtctgggt gtcattgact 29760
tctttccagg ggtcggggga caaggtgggt atctgctgaa cccaaagaaa gcccctgtag 29820
aactggctcc ctaggctctgc ctggccgctt tcagccttgt agccctaggc agagaggaaa 29880
ccaggttgtg ggtgtgaggc aggtgtaccc taaccttatt ctctcctgtc ccctcagtct 29940
tactgtgagc cccctagcta ccggcccatg caccacgagg actttaaaga agacctgaag 30000
aagttccgca ccaagagccg gacctgggca ggggagaaga gcaagaggga gatgtacagt 30060
cgtctgaaga agctctgagg gcggcaggac cagccagcag cagcccaagc ttcctcccat 30120
ccccctttac cctctttgct gcagagaaac ttaagcaag gggacagctg tgtgacattt 30180
ggagaggggg cctgggactt ccatgcctta aacctacct ccacactccc aaggttggag 30240
cccagggcat cttgctggct acgcctcttc tgtccctgtt agacgtctc cgtccatctc 30300
agaactgtgc cacaatgcag ttctgagcac cgtgtcaagc tgctctgagc cacagtggga 30360
tgaaccagcc ggggccttat cgggctccag ccattctcat aggggagagg agacggaggg 30420
gagtagagaa gttacacaga aatgctgctg gccaaatagc aaagacaacc tgggaaggaa 30480
aggtctttgt gggataatcc atatgtttta tttattcaac ttcattcaat actttatttt 30540
atTTTTTTTT ctaactcctg gagacttatt ttactgcttc attaggttga aatactgcca 30600
ttctaggtag ggttttatta tcccaggac tacctcggct tttaatttaa aaaaaaaaaa 30660
gaagtgggta agaaaatgca aacctgttat aagttatcgg acagaaagct aggtgctctg 30720
tcacccccag gaggcgctgt ggtactgggg ctgctgctat ttaagccaag aactgaggtc 30780
ctggtgagag cgttggaacc aggcttggct gcctgacata agctaaatct cccagacca 30840
ccactggcta ccgatatcta tttggtggga ggtgtggccc tggtcttccct caccacagtt 30900
ccatgacatt ggctggtata ggagccacag tcaggaaagc acttgaggca gcatctgttg 30960
ggccaccccc ggctcagtc tggaatgttg cagtgtagggt tcccaggga aggggggtgg 31020
gggtaggtgg gctccacagg atgggggagg agcatgtcca ctgagtatct tccttatgtt 31080
gctgtgatat tgatagcttt tttttctaa tttttaaaaa atggtcatat tatgagtcaa 31140
agagtatcaa atcagtgttg gatggaccac ccaaggggtg ggagaggggc tggaagccct 31200
gggcattagg agaagggagt ggtgctggc atggacatga ctggatagaa ttttctcagg 31260
agggagcttg gtggattttg aaggtaaaac tttctgggtt tatcatgttt taattttaga 31320
gacagggagt gatgaatcat caccggttgt ccccttatct aactccataa aagtgggaat 31380
ttcaaaagaa cacctcatcc aaggagctgg ggcagacttc attgattcta gagagacctg 31440
tttcagtgcc tactcatccc tgccctctgg tgccagctc cttaccatca cggcttcact 31500
gaggtgtagg tgggtttttc ttaaacagga gacagtctct cccctcttac ctcaacttct 31560
tgggggtggga atcagtgata ctggagatgg ctagtgtctg tgttacgggt ttgagttaca 31620
tttggctata aaacaatctt gttgggaaaa atgtggggga gaggacttct tcctacacgc 31680
gcattgagac agattccaac tgggttaatga tattgtttgt aagaaagaga ttctgttggg 31740
tgactgccta aagagaaagg tgggatggcc ttcagattat accagcttag ctagcattac 31800
taaccaactg ttggaagctc tgaaaataaa agatcttgaa cccatgctct ctgcctagtt 31860
cttgatgg
31868

```

<210> 69

<211> 524

<212> PRT

<213> Homo sapiens

<400> 69

```

Met Glu Leu Gly Pro Glu Pro Pro His Arg Arg Arg Leu Leu Phe Ala
1          5          10          15
Cys Ser Pro Pro Pro Ala Ser Gln Pro Val Val Lys Ala Leu Phe Gly
20          25          30

```

Ala	Ser	Ala	Ala	Gly	Gly	Leu	Ser	Pro	Val	Thr	Asn	Leu	Thr	Val	Thr
		35					40					45			
Met	Asp	Gln	Leu	Gln	Gly	Leu	Gly	Ser	Asp	Tyr	Glu	Gln	Pro	Leu	Glu
	50					55					60				
Val	Lys	Asn	Asn	Ser	Asn	Leu	Gln	Arg	Met	Gly	Ser	Ser	Glu	Ser	Thr
65					70					75					80
Asp	Ser	Gly	Phe	Cys	Leu	Asp	Ser	Pro	Gly	Pro	Leu	Asp	Ser	Lys	Glu
				85					90					95	
Asn	Leu	Glu	Asn	Pro	Met	Arg	Arg	Ile	His	Ser	Leu	Pro	Gln	Lys	Leu
			100					105					110		
Leu	Gly	Cys	Ser	Pro	Ala	Leu	Lys	Arg	Ser	His	Ser	Asp	Ser	Leu	Asp
		115					120					125			
His	Asp	Ile	Phe	Gln	Leu	Ile	Asp	Pro	Asp	Glu	Asn	Lys	Glu	Asn	Glu
130						135					140				
Ala	Phe	Glu	Phe	Lys	Lys	Pro	Val	Arg	Pro	Val	Ser	Arg	Gly	Cys	Leu
145					150					155					160
His	Ser	His	Gly	Leu	Gln	Glu	Gly	Lys	Asp	Leu	Phe	Thr	Gln	Arg	Gln
				165					170					175	
Asn	Ser	Ala	Pro	Ala	Arg	Met	Leu	Ser	Ser	Asn	Glu	Arg	Asp	Ser	Ser
		180						185					190		
Glu	Pro	Gly	Asn	Phe	Ile	Pro	Leu	Phe	Thr	Pro	Gln	Ser	Pro	Val	Thr
		195					200					205			
Ala	Thr	Leu	Ser	Asp	Glu	Asp	Asp	Gly	Phe	Val	Asp	Leu	Leu	Asp	Gly
210						215					220				
Glu	Asn	Leu	Lys	Asn	Glu	Glu	Glu	Thr	Pro	Ser	Cys	Met	Ala	Ser	Leu
225					230					235					240
Trp	Thr	Ala	Pro	Leu	Val	Met	Arg	Thr	Thr	Asn	Leu	Asp	Asn	Arg	Cys
				245					250					255	
Lys	Leu	Phe	Asp	Ser	Pro	Ser	Leu	Cys	Ser	Ser	Ser	Thr	Arg	Ser	Val
			260					265					270		
Leu	Lys	Arg	Pro	Glu	Arg	Ser	Gln	Glu	Glu	Ser	Pro	Pro	Gly	Ser	Thr
		275					280					285			
Lys	Arg	Arg	Lys	Ser	Met	Ser	Gly	Ala	Ser	Pro	Lys	Glu	Ser	Thr	Asn
290						295					300				
Pro	Glu	Lys	Ala	His	Glu	Thr	Leu	His	Gln	Ser	Leu	Ser	Leu	Ala	Ser
305					310					315					320
Ser	Pro	Lys	Gly	Thr	Ile	Glu	Asn	Ile	Leu	Asp	Asn	Asp	Pro	Arg	Asp
				325					330					335	
Leu	Ile	Gly	Asp	Phe	Ser	Lys	Gly	Tyr	Leu	Phe	His	Thr	Val	Ala	Gly
			340					345					350		
Lys	His	Gln	Asp	Leu	Lys	Tyr	Ile	Ser	Pro	Glu	Ile	Met	Ala	Ser	Val
		355					360					365			
Leu	Asn	Gly	Lys	Phe	Ala	Asn	Leu	Ile	Lys	Glu	Phe	Val	Ile	Ile	Asp
370						375					380				
Cys	Arg	Tyr	Pro	Tyr	Glu	Tyr	Glu	Gly	Gly	His	Ile	Lys	Gly	Ala	Val
385					390					395					400
Asn	Leu	His	Met	Glu	Glu	Glu	Val	Glu	Asp	Phe	Leu	Leu	Lys	Lys	Pro
				405					410					415	
Ile	Val	Pro	Thr	Asp	Gly	Lys	Arg	Val	Ile	Val	Val	Phe	His	Cys	Glu
			420					425					430		
Phe	Ser	Ser	Glu	Arg	Gly	Pro	Arg	Met	Cys	Arg	Tyr	Val	Arg	Glu	Arg
			435				440					445			
Asp	Arg	Leu	Gly	Asn	Glu	Tyr	Pro	Lys	Leu	His	Tyr	Pro	Glu	Leu	Tyr
450						455					460				
Val	Leu	Lys	Gly	Gly	Tyr	Lys	Glu	Phe	Phe	Met	Lys	Cys	Gln	Ser	Tyr
465					470					475					480
Cys	Glu	Pro	Pro	Ser	Tyr	Arg	Pro	Met	His	His	Glu	Asp	Phe	Lys	Glu
				485					490					495	

Asp Leu Lys Lys Phe Arg Thr Lys Ser Arg Thr Trp Ala Gly Glu Lys
 500 505 510
 Ser Lys Arg Glu Met Tyr Ser Arg Leu Lys Lys Leu
 515 520

<210> 70
 <211> 3415
 <212> DNA
 <213> Rattus norvegicus

<400> 70

```

ctcgcgggac acagagagag aagcaccggg gcttgtgcct ggcgcctgcc gaggccccga 60
cgctcgcccc tccgcgcgcg tgcccggtgg gccgcgctct ctgaaccgcg gggctcgtgtt 120
tgtgttttag ccgcggggcg tggcgcggtg caccgggctga agcgtgcagc ggggcggggg 180
ccggcgcacg gaggcggagg aagacgagcg ggagtcggg caggccccgc ggcgccatgg 240
aactggggcc ggagccccc caccgcgcgc gctgctctt cacttgcagc cccactcctg 300
cgccgcagcc caccgggaag gtgcagtttg gcgcgtcacg tgctggcgga ctgtcccctg 360
tcaccaacct gacggtcacc atggaccagc tgggaagggt gggcagtgac tatgagaaac 420
caatggacgt gagaaatagc agcagtctac agagaatggg ctctctgaa tcgactgatt 480
caggttttctg tctagattct cctgggccc tggacagtaa agaaaacctt gaaatttccc 540
tgaggagaat aaattgccta cctcagaagc tcttgggggt tagcccagcg ctaaagagga 600
gccatttctga ttctctagac caccgacatct ttcaactcat tgaccaggat gaaaataaag 660
aaaatgaagc atttgaattt aaaaagccaa taagacctgc atctcgtggc tgccatgaatg 720
ctcacgttca cgaggaaagt aaggacccct ttacacacag gcagaattca gcccagctc 780
ggatgctgtc ttcaaatgaa agtgacatta gtgaatcagg aaatttcagt cctcttttta 840
caccacagtc acctgtgaaa gcgagtttgt ctgatgagga tgatggcttc atagaccttc 900
tgatgggaga gaatctgaag aatgatgagg agaccgcgtc gtgcatgtca agcctctgga 960
cgctccccct tgtcatgaga agacctacaa accttgccga tcgatgtgga ctgtttgact 1020
ccccctcccc gtgcagctcc accagcagct gcagcactcg ggcagtgaag agagcagacc 1080
gatctcatga ggagtctcct cgaggtacaa agcggaggaa gagcagtgag gccagtccag 1140
tgaaggcaga tgttcgggag ccaacgcagc ttccacacca gtctctctcc ctgacatctt 1200
tccccaaagg aaccattgag aacattttcc acagtaccc aagagacctt ataggggatt 1260
tctccaaagg ttacctctt catacggctc ctgggaagca tcaggatttg aaatatattt 1320
ctccagaaat tatggcatct gttttgaatg gcaagtttgc caatctcatt aaagagtttg 1380
ttatcattga ctgccgatac ccatatgaat atgaaggagg gcacatcaag ggtgccgtga 1440
acttgcacat ggaagaagag gttgaggagt tcttactcaa gaaacctatc gtgcccgctg 1500
acggcaagcg tgtcattgtc gtgttccact gtgagttctc ctctgagaga ggccctcgga 1560
tgtgccgata tgtacgggaa cgagataggc ttggcaatga ataccccaaa ctccactacc 1620
ctgagctgta tgtcctgaag gggggataca aggagttctt tttgaaatgc cagtctcact 1680
gtgaaccccc cagctaccga ccgatgcacc atgaagactt taaagaagac ctaaagaagt 1740
tccgcaccaa gagccggacc tgggcagggg agaagagcaa aaggagatg tacagtcgcc 1800
tgaagaagct ttgaggccaa atggcagtg cctgagcttc cctccgcctt gtccctttgt 1860
ccctttgctg tagagcagta agcaaagggg ccagctatac ggcacctgga ccctggagaa 1920
aaacctgggc ctcccatgcc ttgaacctcc tacactcca ggttgagacc caggcatcct 1980
gccgtcacac tcttctgtga gagtccctcc ctgtcaggac tgtctgcaa agctggacaa 2040
gctcggcaca ggctggcaca ggctcgagtc tagtctggaa cgccacgtca ggctgctccg 2100
actaagcatc ccctgaagaa gtgcccaggc ctctcatgag gggagagaag ccactgaagt 2160
gctgctggcc aaataccaaa gataggctgg aaggggagag gtccctcatg atgactcttt 2220
aatttattca gcctcatcaa ttattttatt attgttttaa ttctcaaga cttttacttt 2280
actgcttcaa agtcaaaaata ctgccattct aggtagagtt ttatcactc aggaactacc 2340
tctactttta atttaaaaaa aaacatggg gcagggataa gaaaaaaggc aaacctgtta 2400
agtgtgggca gcgcaaggaa ctcagtcacc ctaggaggc gctgtagact ggtattgctg 2460
ctattcaaag tcaaggactg agatgctggt cagagcctgc accaaccaga tccaggcttg 2520
gctacaggac ataagctaac cttcccagac ctacttctgc cctttgtgag ttcctttggg 2580
gagagtcttg tctgtactcc tgggtcccagg tccccgtgac agtgactggg gtgggagttg 2640
caggaaggca catcaagcca ccccaggcc agtactggaa tgttgaagtg taccceaagg 2700
tgggagtggt gaggcattga aaagtggagt ccacagagta agggaggagc atgccactg 2760

```

```

aatgtccttt agaaaaaaa aaaagtcatt ttatgagtca gagtatccaa tcagtgttgg 2820
gtgggcacct aagcttgagc agggggcggg aagcccgggc tggtacagac gactgtagaa 2880
tttctcagga gggcgtagta aattttgaag tcaaaagttc tgggtttcat catgttttaa 2940
ttgagggaca gagtggtgaa acacatcagt taccacctaa tctaaccocg tggaagtga 3000
gctctgggga atgcctccca tctaaggagc tggcccgttt tgattctgtc agtgcctc 3060
ggcaccagcc tcctgccat ctgtgtccca ttgggggtcat gccaggtttt tcttaggaag 3120
agtctccctt cttaacctct gctttctatt ctgggggttg ggaggggaatc aatgatattg 3180
aagatggcta gttgctttgt taagggtttg agtttgcatt tggctataaa acaaattctg 3240
ttaaaaatat gtggagagca agggaatgag cagcctcttc ttcggtgtgt tgaagtatgt 3300
cctagttttc ccctggtctg gttttagtag attctgttag ttgaatgcct tcaaggagaa 3360
tgaatggctt tcagattgta ccagcttagc tagcattgtt aaccagctgc tgcag 3415

```

<210> 71

<211> 525

<212> PRT

<213> Rattus norvegicus

<400> 71

```

Met Glu Leu Gly Pro Glu Pro Pro His Arg Arg Arg Leu Leu Phe Thr
 1          5          10          15
Cys Ser Pro Thr Pro Ala Pro Gln Pro Thr Gly Lys Val Gln Phe Gly
          20          25          30
Ala Ser Arg Ala Gly Gly Leu Ser Pro Val Thr Asn Leu Thr Val Thr
          35          40          45
Met Asp Gln Leu Glu Gly Leu Gly Ser Asp Tyr Glu Lys Pro Met Asp
          50          55          60
Val Arg Asn Ser Ser Ser Leu Gln Arg Met Gly Ser Ser Glu Ser Thr
          65          70          75          80
Asp Ser Gly Phe Cys Leu Asp Ser Pro Gly Pro Leu Asp Ser Lys Glu
          85          90          95
Asn Leu Glu Ile Ser Leu Arg Arg Ile Asn Cys Leu Pro Gln Lys Leu
          100          105          110
Leu Gly Cys Ser Pro Ala Leu Lys Arg Ser His Ser Asp Ser Leu Asp
          115          120          125
His Asp Ile Phe Gln Leu Ile Asp Gln Asp Glu Asn Lys Glu Asn Glu
          130          135          140
Ala Phe Glu Phe Lys Lys Pro Ile Arg Pro Ala Ser Arg Gly Cys Leu
          145          150          155          160
Asn Ala His Val His Glu Glu Ser Lys Asp Pro Phe Thr His Arg Gln
          165          170          175
Asn Ser Ala Pro Ala Arg Met Leu Ser Ser Asn Glu Ser Asp Ile Ser
          180          185          190
Glu Ser Gly Asn Phe Ser Pro Leu Phe Thr Pro Gln Ser Pro Val Lys
          195          200          205
Ala Ser Leu Ser Asp Glu Asp Asp Gly Phe Ile Asp Leu Leu Asp Gly
          210          215          220
Glu Asn Leu Lys Asn Asp Glu Glu Thr Pro Ser Cys Met Ser Ser Leu
          225          230          235          240
Trp Thr Ala Pro Leu Val Met Arg Arg Pro Thr Asn Leu Ala Asp Arg
          245          250          255
Cys Gly Leu Phe Asp Ser Pro Ser Pro Cys Ser Ser Thr Ser Ser Cys
          260          265          270
Ser Thr Arg Ala Val Lys Arg Ala Asp Arg Ser His Glu Glu Ser Pro
          275          280          285
Arg Gly Thr Lys Arg Arg Lys Ser Ser Glu Ala Ser Pro Val Lys Ala
          290          295          300
Asp Val Pro Glu Pro Thr Gln Leu Pro His Gln Ser Leu Ser Leu Thr
          305          310          315          320

```

Ser Phe Pro Lys Gly Thr Ile Glu Asn Ile Phe His Ser Asp Pro Arg
 325 330 335
 Asp Leu Ile Gly Asp Phe Ser Lys Gly Tyr Leu Phe His Thr Val Ser
 340 345 350
 Gly Lys His Gln Asp Leu Lys Tyr Ile Ser Pro Glu Ile Met Ala Ser
 355 360 365
 Val Leu Asn Gly Lys Phe Ala Asn Leu Ile Lys Glu Phe Val Ile Ile
 370 375 380
 Asp Cys Arg Tyr Pro Tyr Glu Tyr Glu Gly Gly His Ile Lys Gly Ala
 385 390 395 400
 Val Asn Leu His Met Glu Glu Glu Val Glu Glu Phe Leu Leu Lys Lys
 405 410 415
 Pro Ile Val Pro Ala Asp Gly Lys Arg Val Ile Val Val Phe His Cys
 420 425 430
 Glu Phe Ser Ser Glu Arg Gly Pro Arg Met Cys Arg Tyr Val Arg Glu
 435 440 445
 Arg Asp Arg Leu Gly Asn Glu Tyr Pro Lys Leu His Tyr Pro Glu Leu
 450 455 460
 Tyr Val Leu Lys Gly Gly Tyr Lys Glu Phe Phe Leu Lys Cys Gln Ser
 465 470 475 480
 His Cys Glu Pro Pro Ser Tyr Arg Pro Met His His Glu Asp Phe Lys
 485 490 495
 Glu Asp Leu Lys Lys Phe Arg Thr Lys Ser Arg Thr Trp Ala Gly Glu
 500 505 510
 Lys Ser Lys Arg Glu Met Tyr Ser Arg Leu Lys Lys Leu
 515 520 525

<210> 72

<211> 2804

<212> DNA

<213> Rattus norvegicus

<400> 72

```

gggggggggg ttatttttctg aatatataag gaggtggagg tggcagcagc ccagctcgcg 60
tcttccccctc ccttctctccc cacatccctc tctcactcc caggcccact gctcttctctc 120
cctccccctcc ctccctcctt ccccttacct caggctcact ctcgagacct agccagctgg 180
gtcggcgctct gctggcgcggt tatcttgtgg ccctctagct agcctttgcc cgccccgcca 240
ccatggagggt acccccgagc aagtctgcgc cgggctcagc tctcagtaact gcccgcgtgc 300
tgggtggcat tcagcggccg cgccacctct caggctttgg gtttgggtct gatggcttgc 360
tgggggtctcc agagcgtgcg gcttctctct ctccgggttac cactcttacc cagaccatgt 420
acaacctcgc agggctcggc agcgagaccc caaaaactca agtaggaagc ctgtcgttcc 480
agaacagggt gacagacctg tccctgtcca gacgtacctc tgagtgtctc ctgtcatctg 540
agtcctcaga atcttctgat gcaggctctc gcatggactc ccctagccct atggaccac 600
agacagcaga gcgcacgttt gaacaggcca ttcaggcagc cagtcgggtc attcaaaaga 660
tgcaatttac cataaaagct tcggtctttg ccagtggagg tgctggacat agtcctgtgc 720
tacagaacat caccaactcc caagcactgg acagctggga gaaagatgaa gcaggctaca 780
gagctgccag tagtcctggg gaggacaaag agaacgatgg atatatcttc aagatgccac 840
agaagctccc tcattccagc tctgcccag ctttggcaga gtgggcccagc cgcagagagg 900
cctttaccga gagggccagc tcagcccctg acttgatgtg tcttaccact gacgggaaga 960
tggacgtgga ggaggcgagc cctgtggcac agtcttcctc cttgactcct gtcgaaaggg 1020
cttgtgaaga agatgacgga tttgtggaca tcctagagag tgatttaaag gatgatgata 1080
tgggtccccgc aggcatggag aacctcatta gtgctccact ggtcaaaaag ctggataagg 1140
aagaggaaca ggatctcatc atgttcagca agtgccagcg gcttttccgc tctccatcca 1200
tgccgtgcag tgtgatccgg cccatcctca agaggctaga gcggcccccac gacaggggacg 1260
tgccgtgctc gagcaagcgc aggaagagtg ggacaccctt ggaagagcag cagcttgaag 1320
aaccgaaggc ccgggtcttc cgctcaaagt ccctgtgtca cgagattgag agcatcctgg 1380
acagtgacca ccgtggcctg attggagatt actctaaggc cttcctcctg cagactgtgg 1440

```



```

atggcaaaca ccaagacctc aagtacatct caccagaaac tatggtggcc ctgttgacag 1500
gcaagttcag caacatcggt gagaagtttg taattgtgga ctgcagatac ccctatgagt 1560
atgaaggcgg gcatatcaag aatgctgtga acttgcccct ggaaccggat gccgagacct 1620
ttctgctgaa gcatcccatc acgccttgta acctggacaa gagaatcatc ctcattttcc 1680
actgtgaatt ctcactctgag cgtggaccac ggatgtgccg cttcatcagg gaacgggacc 1740
gtgcagctaa cgactatccc agcctgtact accctgagat gtacatcctc aaaggcggct 1800
acaaggagtt cttcccgagc catccgaact tttgtgagcc ccaggactac cgacccatga 1860
accatgcagc tttccgggat gagctgagga acttccgcct caagacacgc agctgggctg 1920
gggaacggag taccacccaa ctctgtagca ggctgcaaga ccagtacga gccagcctca 1980
gtcctgccac catccttacc tcaggaggct tgccagccag tgggtcccat gggcctatgc 2040
ggccacctac ttgctagagg cctcagggtc tatagggggt tggggggatg gtgtggtgtc 2100
acatctgtct gtccctgtcc tcaattttcc tgtctcactc cactaatttt ctgtatcttg 2160
gatctgatcc catcttaaag agctgaacca atgggtgaat accagctaag aggaagtcct 2220
ttgtgttcaa tgagagccct tttacaatct cttttttcct tgtttgtgtt gactccttgt 2280
cttacccttt cgcagggaga gcctcagccc tttaagatga gcacagtagc ttcttgggta 2340
gcctggattg caggagccta cactgctgca cagggtgtgt tctgctctcc tctcctggcc 2400
tctgcacaga ttccctccatt ggaagcataa gtgcttagtt tcctgttgtc gtcttaccga 2460
tagctttcat tttcgtctgt ctcacttagc gtgtcccagg acacactgac agctggggag 2520
gctcccttgt acagctgggg actagagatt caaatatcat gtactcatta ggcttggctt 2580
ttgttagccc acaaagggat ctttttccttt aagaccccca gagctagagc aaaggcctga 2640
ttcaggagcc tctgggagcc ccctcctcac tgctgtgaac cctagagcct cactggtcag 2700
cacttggtgc tgggcaatga accagtcact gagcttcaact ttttggtcct tctctgtccc 2760
tccctgtccc tctctgtcct tctttccata tctggtcctg agta 2804

```

<210> 73

<211> 574

<212> PRT

<213> Rattus norvegicus

<400> 73

```

Met Glu Val Pro Pro Gln Lys Ser Ala Pro Gly Ser Ala Leu Ser Thr
1          5          10          15
Ala Arg Val Leu Gly Gly Ile Gln Arg Pro Arg His Leu Ser Gly Phe
20          25          30
Gly Phe Gly Ser Asp Gly Leu Leu Gly Ser Pro Glu Arg Ala Ala Ser
35          40          45
Ser Ser Pro Val Thr Thr Leu Thr Gln Thr Met Tyr Asn Leu Ala Gly
50          55          60
Leu Gly Ser Glu Thr Pro Lys Thr Gln Val Gly Ser Leu Ser Phe Gln
65          70          75          80
Asn Arg Leu Thr Asp Leu Ser Leu Ser Arg Arg Thr Ser Glu Cys Ser
85          90          95
Leu Ser Ser Glu Ser Ser Glu Ser Ser Asp Ala Gly Leu Cys Met Asp
100         105         110
Ser Pro Ser Pro Met Asp Pro Gln Thr Ala Glu Arg Thr Phe Glu Gln
115         120         125
Ala Ile Gln Ala Ala Ser Arg Val Ile Gln Lys Met Gln Phe Thr Ile
130         135         140
Lys Ala Ser Val Phe Ala Ser Glu Ala Ala Gly His Ser Pro Val Leu
145         150         155         160
Gln Asn Ile Thr Asn Ser Gln Ala Leu Asp Ser Trp Glu Lys Asp Glu
165         170         175
Ala Gly Tyr Arg Ala Ala Ser Ser Pro Gly Glu Asp Lys Glu Asn Asp
180         185         190
Gly Tyr Ile Phe Lys Met Pro Gln Lys Leu Pro His Ser Ser Ser Ala
195         200         205
Arg Ala Leu Ala Glu Trp Ala Ser Arg Arg Glu Ala Phe Thr Gln Arg
210         215         220

```

Pro Ser Ser Ala Pro Asp Leu Met Cys Leu Thr Thr Asp Gly Lys Met
 225 230 235 240
 Asp Val Glu Glu Ala Ser Pro Val Ala Gln Ser Ser Ser Leu Thr Pro
 245 250 255
 Val Glu Arg Ala Cys Glu Glu Asp Asp Gly Phe Val Asp Ile Leu Glu
 260 265 270
 Ser Asp Leu Lys Asp Asp Asp Met Val Pro Ala Gly Met Glu Asn Leu
 275 280 285
 Ile Ser Ala Pro Leu Val Lys Lys Leu Asp Lys Glu Glu Gln Asp
 290 295 300
 Leu Ile Met Phe Ser Lys Cys Gln Arg Leu Phe Arg Ser Pro Ser Met
 305 310 315 320
 Pro Cys Ser Val Ile Arg Pro Ile Leu Lys Arg Leu Glu Arg Pro His
 325 330 335
 Asp Arg Asp Val Pro Val Leu Ser Lys Arg Arg Lys Ser Gly Thr Pro
 340 345 350
 Leu Glu Glu Gln Gln Leu Glu Glu Pro Lys Ala Arg Val Phe Arg Ser
 355 360 365
 Lys Ser Leu Cys His Glu Ile Glu Ser Ile Leu Asp Ser Asp His Arg
 370 375 380
 Gly Leu Ile Gly Asp Tyr Ser Lys Ala Phe Leu Leu Gln Thr Val Asp
 385 390 395 400
 Gly Lys His Gln Asp Leu Lys Tyr Ile Ser Pro Glu Thr Met Val Ala
 405 410 415
 Leu Leu Thr Gly Lys Phe Ser Asn Ile Val Glu Lys Phe Val Ile Val
 420 425 430
 Asp Cys Arg Tyr Pro Tyr Glu Tyr Glu Gly Gly His Ile Lys Asn Ala
 435 440 445
 Val Asn Leu Pro Leu Glu Pro Asp Ala Glu Thr Phe Leu Leu Lys His
 450 455 460
 Pro Ile Thr Pro Cys Asn Leu Asp Lys Arg Ile Ile Leu Ile Phe His
 465 470 475 480
 Cys Glu Phe Ser Ser Glu Arg Gly Pro Arg Met Cys Arg Phe Ile Arg
 485 490 495
 Glu Arg Asp Arg Ala Ala Asn Asp Tyr Pro Ser Leu Tyr Tyr Pro Glu
 500 505 510
 Met Tyr Ile Leu Lys Gly Gly Tyr Lys Glu Phe Phe Pro Gln His Pro
 515 520 525
 Asn Phe Cys Glu Pro Gln Asp Tyr Arg Pro Met Asn His Ala Ala Phe
 530 535 540
 Arg Asp Glu Leu Arg Asn Phe Arg Leu Lys Thr Arg Ser Trp Ala Gly
 545 550 555 560
 Glu Arg Ser Thr Thr Gln Leu Cys Ser Arg Leu Gln Asp Gln
 565 570

<210> 74

<211> 2935

<212> DNA

<213> Mus musculus

<400> 74

tcccctcacc ccaggctcac tctcggagct gagccagctg ggtcggcgctc tgctggccgc 60
 tgtactgtgg ccctctagct agcctttgcc cgccccgcca cgatggagggt acccctgcag 120
 aagtctgcgc cgggttcagc tctcagtcct gcccgctgc tgggtggcat tcagcggccg 180
 cgccacctct cgggttttga gtttgagtct gatggcttcc tggggtctcc ggagcctaca 240
 gcttctcct ctccggttac cactcttaca cagaccatgc acaacctcgc tgggctcggc 300
 agtgagcctc caaaagctca agtaggaagc ctgtcgttcc agaacaggct ggcagacct 360

```

tccctgtcca ggcgacacct tgagtgtccc ctgtcatctg agtcctcaga atcttcggat 420
gcaggtctgt gcatggactc cccagccct gtggaccgc agatggcaga gcgcacgttt 480
gaacaggcca ttcaggcagc cagtcgggtc attcaaatg agcagtttac cataaacgc 540
ttccgatcct taccagttag gctgctggaa cacagtccgg tgctgcagag catcaccaac 600
tcccagacac tggacagctg gaggaaaact gaagcaggct accgagccgc cgccaatagt 660
cctggggagg acaaagagaa tgatggatat atcttcaaga tgccacagga gtcctctcat 720
tccagctctg cccaagcttt ggcagaatgg gtcagccgca gacaggcctt taccagagg 780
cccagctcag cccctgactt gatgtgtctt accactgagt ggaagatgga agtagaggag 840
ctgagcccgg tggcacagtc ttcttccttg actcctgtcg aaagggttc tgaagaagat 900
gacggatttg tggacatcct ggagagtgat ttaaaggatg acgagaaggt ccccgcgggc 960
atggagaacc tcattagtgc cccactggtc aaaaagctgg ataaggaaga ggaacaggat 1020
ctcatcatgt tcagcaagtg ccagaggctc ttccgctccc catccatgcc atgcagtgtg 1080
atccgaccca tcctcaagag gctagagcgg cccaggacc gggatgtgcc tgtccagagc 1140
aagcgagga aaagtgtgac acccctggaa gagcagcagc ttgaagaacc taaggcccgt 1200
gtctttcgct caaagtcgct gtgtcatgag attgagaaca tcctggatag tgaccaccgt 1260
ggactgatcg gagattactc taaggccttc ctctgcaga ccgtggatgg caaacaccaa 1320
gaccttaagt acatctcacc agaaactatg gtggccctgt taacaggcaa gttcagcaac 1380
atcgtggaga aatttgtcat tgtggactgc agataccct atgagtatga aggggggcat 1440
atcaagaatg ctgtgacct gccctggaa cgggatgtcg agacctttct gctgcagcgt 1500
cccatcatgc cttgtagcct ggacaagaga atcatctca ttttccactg tgaattctcg 1560
tctgagcgtg gaccacgaat gtgccgcttc atcagggaac gggaccgtgc agctaacgac 1620
taccagacc tgtactacc ggagatgtac atcctcaaag gcggctacaa ggagttcttc 1680
ccacagcatc cgaacttttg tgagccccag gactaccgac ccatgaacca cgaggcttct 1740
agggatgagc tgaggaactt tcgcttaag actcgcagct gggctgggga acggagcagg 1800
agggaaactt gtagcaggct gcaagaccag tgatgatgag cctgctgcca tccttacctc 1860
gtgaggcttg ggagccagtg ggtcccatgg gcctgtgagg ccacctacct tatagaggcc 1920
tcaggtgcta tagggggttg ggggcatggt gtggtgtcac atctgtctgc cctgtctc 1980
aattttcctg tctactcca cttatttct gtatcttgg actggtccca gcttaaagag 2040
ctgaacctga ggggtgatgc cagctgagga gaagtctgt gtgttcagtg ggagtccttt 2100
tacagtcttt ttctctgtt tgtgttgact ctttgtcttc ccgctttttg gggagagcct 2160
cagccccgtt aggatggcac agtagcttct tgcatggcct ggatgcagga tgctactctg 2220
ctacacaggg ctgtgtctac tctcctctcc tggccactgg catagactta tgctctccat 2280
tggaagcata agtggcttct tctctgttg tagtcttacc tgtagcttct atttttttgt 2340
ctgtctgaca cactgaccgc tggggaggct tccttgtaca gcttggggct agagattcaa 2400
atatcactta ctggttaggc ctggcttttg ttagccaga aagggatctt gccctttaag 2460
accccaggg ctagagggaa ggcctgactc aggagcctct gggagcccca tcctcactac 2520
tgtgaacccc agagcctcgc tggtcagcac ttgctgtg gcaatggacc agtcaccgag 2580
ctttgctgtt tgatccttct ctgcccttc ctgttttct tctatatct ggcccagaag 2640
acctcttgta tgtgtggttt ttctgtgtg tactagtac ttgagtctag gccctttgtt 2700
gcatggtcat ggatgcacag tgccttatat acatgtatgc acacaaaccg ggtccaagta 2760
ttttggttaag catgatggcc tatggcagga gtgtgtgtgt gcgctgtga acaaagtc 2820
tacacttagt gtttggaat gttaaagaag cattgttatt atggggagg gggagcaacc 2880
tctgggttca gaatctacat atgctggaag gcccacatga gtcctctgtt ggggg 2935

```

<210> 75

<211> 576

<212> PRT

<213> Mus musculus

<400> 75

```

Met Glu Val Pro Leu Gln Lys Ser Ala Pro Gly Ser Ala Leu Ser Pro
1          5          10          15
Ala Arg Val Leu Gly Gly Ile Gln Arg Pro Arg His Leu Ser Val Phe
20          25          30
Glu Phe Glu Ser Asp Gly Phe Leu Gly Ser Pro Glu Pro Thr Ala Ser
35          40          45
Ser Ser Pro Val Thr Thr Leu Thr Gln Thr Met His Asn Leu Ala Gly
50          55          60

```

Leu Gly Ser Glu Pro Pro Lys Ala Gln Val Gly Ser Leu Ser Phe Gln
 65 70 75 80
 Asn Arg Leu Ala Asp Leu Ser Leu Ser Arg Arg Thr Ser Glu Cys Ser
 85 90 95
 Leu Ser Ser Glu Ser Ser Glu Ser Ser Asp Ala Gly Leu Cys Met Asp
 100 105 110
 Ser Pro Ser Pro Val Asp Pro Gln Met Ala Glu Arg Thr Phe Glu Gln
 115 120 125
 Ala Ile Gln Ala Ala Ser Arg Val Ile Gln Asn Glu Gln Phe Thr Ile
 130 135 140
 Lys Arg Phe Arg Ser Leu Pro Val Arg Leu Leu Glu His Ser Pro Val
 145 150 155 160
 Leu Gln Ser Ile Thr Asn Ser Arg Ala Leu Asp Ser Trp Arg Lys Thr
 165 170 175
 Glu Ala Gly Tyr Arg Ala Ala Ala Asn Ser Pro Gly Glu Asp Lys Glu
 180 185 190
 Asn Asp Gly Tyr Ile Phe Lys Met Pro Gln Glu Leu Pro His Ser Ser
 195 200 205
 Ser Ala Gln Ala Leu Ala Glu Trp Val Ser Arg Arg Gln Ala Phe Thr
 210 215 220
 Gln Arg Pro Ser Ser Ala Pro Asp Leu Met Cys Leu Thr Thr Glu Trp
 225 230 235 240
 Lys Met Glu Val Glu Glu Leu Ser Pro Val Ala Gln Ser Ser Ser Leu
 245 250 255
 Thr Pro Val Glu Arg Ala Ser Glu Glu Asp Asp Gly Phe Val Asp Ile
 260 265 270
 Leu Glu Ser Asp Leu Lys Asp Asp Glu Lys Val Pro Ala Gly Met Glu
 275 280 285
 Asn Leu Ile Ser Ala Pro Leu Val Lys Lys Leu Asp Lys Glu Glu Glu
 290 295 300
 Gln Asp Leu Ile Met Phe Ser Lys Cys Gln Arg Leu Phe Arg Ser Pro
 305 310 315 320
 Ser Met Pro Cys Ser Val Ile Arg Pro Ile Leu Lys Arg Leu Glu Arg
 325 330 335
 Pro Gln Asp Arg Asp Val Pro Val Gln Ser Lys Arg Arg Lys Ser Val
 340 345 350
 Thr Pro Leu Glu Glu Gln Gln Leu Glu Glu Pro Lys Ala Arg Val Phe
 355 360 365
 Arg Ser Lys Ser Leu Cys His Glu Ile Glu Asn Ile Leu Asp Ser Asp
 370 375 380
 His Arg Gly Leu Ile Gly Asp Tyr Ser Lys Ala Phe Leu Leu Gln Thr
 385 390 395 400
 Val Asp Gly Lys His Gln Asp Leu Lys Tyr Ile Ser Pro Glu Thr Met
 405 410 415
 Val Ala Leu Leu Thr Gly Lys Phe Ser Asn Ile Val Glu Lys Phe Val
 420 425 430
 Ile Val Asp Cys Arg Tyr Pro Tyr Glu Tyr Glu Gly Gly His Ile Lys
 435 440 445
 Asn Ala Val Asn Leu Pro Leu Glu Arg Asp Ala Glu Thr Phe Leu Leu
 450 455 460
 Gln Arg Pro Ile Met Pro Cys Ser Leu Asp Lys Arg Ile Ile Leu Ile
 465 470 475 480
 Phe His Cys Glu Phe Ser Ser Glu Arg Gly Pro Arg Met Cys Arg Phe
 485 490 495
 Ile Arg Glu Arg Asp Arg Ala Ala Asn Asp Tyr Pro Ser Leu Tyr Tyr
 500 505 510
 Pro Glu Met Tyr Ile Leu Lys Gly Gly Tyr Lys Glu Phe Phe Pro Gln
 515 520 525

His	Pro	Asn	Phe	Cys	Glu	Pro	Gln	Asp	Tyr	Arg	Pro	Met	Asn	His	Glu
530						535					540				
Ala	Phe	Arg	Asp	Glu	Leu	Arg	Asn	Phe	Arg	Leu	Lys	Thr	Arg	Ser	Trp
545					550					555					560
Ala	Gly	Glu	Arg	Ser	Arg	Arg	Glu	Leu	Cys	Ser	Arg	Leu	Gln	Asp	Gln
				565					570						575

<210> 76
 <211> 3578
 <212> DNA
 <213> Homo sapiens

<400> 76

gcagccagtc	gcggaggcgg	ggaggctgcg	cggctcagagg	cgccctggagc	gagcgaatcc	60
tggcccaccg	cctgcccac	cgctgacct	tgattgagtt	aatgaacttc	acgcctcagc	120
gtccaggctc	gtaaaatggg	gtgtctaacg	cagaccgtac	agcccagctg	ggtttagcaa	180
acttccggga	gccagttgga	gcctctcccc	atccctagcg	gtgatcccag	gtgacgacat	240
gccgcggggg	gtcctgcgga	ggccacccta	ggcggttgct	gctgcctttg	ggagtgtgga	300
gctccaaacc	atgtcgcgag	aggcggattt	tgggaggccg	ggatcctcgc	gccaggggga	360
tgtgcgaggg	tgtgggataa	atcttaattc	ctccggccca	cccaaagcct	ggaaatccag	420
cctccgcgcc	tcttgccctg	cgggccccgc	cctcagtcct	gccctcatct	aaccgcgtac	480
cccattggtg	gcgtccggcg	gcgcggctgc	tgttatTTTT	cgaatatata	aggaggtgga	540
agtggcagct	gcaactagag	gcttccttgg	ctgggtgcctg	agcccggcgt	ccctcgcccc	600
ccgcccctcc	cgcctccctc	tcctccctcg	cgccctggccc	tgtggctctt	cctccctccc	660
tccttcccc	cccccccacc	cctcgcccg	tgccctccct	ggcccagcca	gctgtgccgg	720
cgtttgttgg	ctgccctgcg	cccgccctc	cagccagcct	tctgccggcc	ccgcgcgat	780
ggaggtgccc	cagccggagc	ccgcgccagg	ctcggctctc	agtccagcag	gcgtgtgcgg	840
tggcgcccag	cgtccggggc	acctcccggg	cctcctgctg	ggatctcatg	gcctcctggg	900
gtccccggtg	cgggcgggcg	cttcctcgcc	ggtcaccacc	ctcaccacga	ccatgcacga	960
cctcgccggg	ctcggcagcg	aaacccccaa	gagtcaggta	gggaccctgc	tcttcgcgag	1020
ccgcagccgc	ctgacgcacc	tatccctgtc	tcgacgggca	tccgaatcct	ccctgtcgtc	1080
tgaatcctcc	gaatcttctg	atgcaggctc	ctgcatggat	tccccagcc	ctatggaccc	1140
ccacatggcg	gagcagacgt	ttgaacaggc	catccaggca	gccagccgga	tcattcgaaa	1200
cgagcagttt	gccatcagac	gcttcagtc	tatgccggat	ggatttgtct	tcaagatgcc	1260
atggaagccc	acacatccca	gctccacca	tgctctggca	gagtgggcca	gccgcaggga	1320
agcctttgcc	cagagaccca	gctcggcccc	cgactgtatg	tgtctcagtc	ctgaccggaa	1380
gatggaagtg	gaggagctca	gccccctggc	ccatggctgc	ttctctctga	cccctgcaga	1440
gggggatact	gaggaagatg	atggatttgt	ggacatccta	gagagtgact	taaaggatga	1500
tgatgcagtt	ccccaggca	tggagagtct	cattagtgcc	ccactggtca	agaccttga	1560
aaaggaagag	gaaaaggacc	tcgtcatgta	cagcaagtgc	cagcggctct	tccgtctctc	1620
gtccatgccc	tgcagcgtga	tccggcccat	cctcaagagg	ctggagcggc	cccaggacag	1680
ggacacgccc	gtgcagaata	agcggaggcg	gagcgtgacc	cctcctgagg	agcagcagga	1740
ggctgaggaa	cctaaagccc	gcgtcctccg	ctcaaaatca	ctgtgtcacg	atgagatcga	1800
gaacctcctg	gacagtgacc	accgagagct	gattggagat	tactctaagg	ccttcctcct	1860
acagacagta	gacggaaagc	accaagacct	caagtacatc	tcaccagaaa	cgatgggtgg	1920
cctattgacg	ggcaagtcca	gcaacatcgt	ggataagttt	gtgattgtag	actgcagata	1980
cccctatgaa	tatgaaggcg	ggcacatcaa	gactgcggtg	aacttgcccc	tggaaacgca	2040
cgccgagagc	ttcctactga	agagcccat	cgccgctgt	agcctggaca	agagagtcac	2100
cctcatTTTT	cactgtgaat	tctcatctga	gcgtgggccc	cgcatgtgcc	gtttcatcag	2160
ggaacgagac	cgtgctgtca	acgactaccc	cagcctctac	tacctgaga	tgtatatcct	2220
gaaaggcggc	tacaaggagt	tcttccctca	gcacccgaac	ttctgtgaac	cccaggacta	2280
ccggccccatg	aaccacgagg	ccttcaagga	tgagctaaag	accttccgcc	tcaagactcg	2340
cagctgggct	gggggcgga	gccggcgga	gctctgtagc	cggctgcagg	accagttagg	2400
ggcctgcgcc	agtcctgtca	cctcccttgc	cttctgaggc	ctgaagccag	ctgccctatg	2460
ggcctgccgg	gctgaggggc	tgctggaggc	ctcaggtgct	gtccatggga	aagatgggtg	2520
gggtgtcctg	cctgtctgcc	ccagcccaga	ttccctgtg	tcaccccatc	atTTTccata	2580
tcctggtgcc	ccccaccct	ggaagagccc	agtctgttga	gttagttaag	ttgggttaat	2640

```

accagcttaa aggcagtatt ttgtgtcctc caggagcttc ttgtttcctt gttagggtta 2700
acccttcac ttcctgtgtc ctgaaacgct cctttgtgtg tgtgtcagct gaggctgggg 2760
gagagccgtg gtccttgagg atgggtcaga gctaaactcc ttcttggcct gagagtcagc 2820
tctctgccct gtgtacttcc cgggccaggg ctgccctaa tctctgtagg aaccgtggta 2880
tgtctgccat gttgcccctt tctcttttcc cctttcctgt cccaccatac gagcacctcc 2940
agcctgaaca gaagctctta ctctttccta tttcagtgtt acctgtgtgc ttggtctgtt 3000
tgactttacg cccatctcag gacacttccg tagactgttt aggttcccct gtcaaataac 3060
agttaccac tcggtcccag ttttgttgcc ccagaaaggg atgttattat ccttgggggc 3120
tcccagggca agggtaagg cctgaatcat gagcctgctg gaagcccagc ccctactgct 3180
gtgaaccctg gggcctgact gctcagaact tgctgtgtgc ttgttgcgga tggatggaag 3240
gttggatgga tgggtggatg gccgtggatg gccgtggatg cgcagtgcct tgcataccca 3300
aaccaggtgg gagcgttttg ttgagcatga cagcctgcag caggaatata tgtgtgccta 3360
tttgtgtgga caaaaatatt tacacttagg gtttggagct attcaagagg aaatgtcaca 3420
gaagcagcta aaccaaggac tgagcacctt ctggattctg aatctcaaga tgggggcagg 3480
gctgtgcttg aaggccctgc tgagtcactt gttagggcct tggttcaata aagcactgag 3540
caagttgaga aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 3578

```

<210> 77

<211> 539

<212> PRT

<213> Homo sapiens

<400> 77

```

Met Glu Val Pro Gln Pro Glu Pro Ala Pro Gly Ser Ala Leu Ser Pro
1          5          10          15
Ala Gly Val Cys Gly Gly Ala Gln Arg Pro Gly His Leu Pro Gly Leu
20          25          30
Leu Leu Gly Ser His Gly Leu Leu Gly Ser Pro Val Arg Ala Ala Ala
35          40          45
Ser Ser Pro Val Thr Thr Leu Thr Gln Thr Met His Asp Leu Ala Gly
50          55          60
Leu Gly Ser Glu Thr Pro Lys Ser Gln Val Gly Thr Leu Leu Phe Arg
65          70          75          80
Ser Arg Ser Arg Leu Thr His Leu Ser Leu Ser Arg Arg Ala Ser Glu
85          90          95
Ser Ser Leu Ser Ser Glu Ser Ser Glu Ser Ser Asp Ala Gly Leu Cys
100          105          110
Met Asp Ser Pro Ser Pro Met Asp Pro His Met Ala Glu Gln Thr Phe
115          120          125
Glu Gln Ala Ile Gln Ala Ala Ser Arg Ile Ile Arg Asn Glu Gln Phe
130          135          140
Ala Ile Arg Arg Phe Gln Ser Met Pro Asp Gly Phe Val Phe Lys Met
145          150          155          160
Pro Trp Lys Pro Thr His Pro Ser Ser Thr His Ala Leu Ala Glu Trp
165          170          175
Ala Ser Arg Arg Glu Ala Phe Ala Gln Arg Pro Ser Ser Ala Pro Asp
180          185          190
Leu Met Cys Leu Ser Pro Asp Arg Lys Met Glu Val Glu Glu Leu Ser
195          200          205
Pro Leu Ala Leu Gly Arg Phe Ser Leu Thr Pro Ala Glu Gly Asp Thr
210          215          220
Glu Glu Asp Asp Gly Phe Val Asp Ile Leu Glu Ser Asp Leu Lys Asp
225          230          235          240
Asp Asp Ala Val Pro Pro Gly Met Glu Ser Leu Ile Ser Ala Pro Leu
245          250          255
Val Lys Thr Leu Glu Lys Glu Glu Glu Lys Asp Leu Val Met Tyr Ser
260          265          270
Lys Cys Gln Arg Leu Phe Arg Ser Pro Ser Met Pro Cys Ser Val Ile

```

275	280	285
Arg Pro Ile Leu Lys Arg	Leu Glu Arg Pro Gln Asp	Arg Asp Thr Pro
290	295	300
Val Gln Asn Lys Arg	Arg Arg Ser Val Thr Pro	Pro Glu Glu Gln Gln
305	310	315
Glu Ala Glu Glu Pro	Lys Ala Arg Val Leu Arg	Ser Lys Ser Leu Cys
325	330	335
His Asp Glu Ile Glu	Asn Leu Leu Asp Ser Asp	His Arg Glu Leu Ile
340	345	350
Gly Asp Tyr Ser Lys	Ala Phe Leu Leu Gln Thr	Val Asp Gly Lys His
355	360	365
Gln Asp Leu Lys Tyr	Ile Ser Pro Glu Thr Met	Val Ala Leu Leu Thr
370	375	380
Gly Lys Phe Ser Asn	Ile Val Asp Lys Phe Val	Ile Val Asp Cys Arg
385	390	395
Tyr Pro Tyr Glu Tyr	Glu Gly Gly His Ile Lys	Thr Ala Val Asn Leu
405	410	415
Pro Leu Glu Arg Asp	Ala Glu Ser Phe Leu Leu	Lys Ser Pro Ile Ala
420	425	430
Pro Cys Ser Leu Asp	Lys Arg Val Ile Leu Ile	Phe His Cys Glu Phe
435	440	445
Ser Ser Glu Arg Gly	Pro Arg Met Cys Arg Phe	Ile Arg Glu Arg Asp
450	455	460
Arg Ala Val Asn Asp	Tyr Pro Ser Leu Tyr Tyr	Pro Glu Met Tyr Ile
465	470	475
Leu Lys Gly Gly Tyr	Lys Glu Phe Phe Pro Gln	His Pro Asn Phe Cys
485	490	495
Glu Pro Gln Asp Tyr	Arg Pro Met Asn His Glu	Ala Phe Lys Asp Glu
500	505	510
Leu Lys Thr Phe Arg	Leu Lys Thr Arg Ser Trp	Ala Gly Glu Arg Ser
515	520	525
Arg Arg Glu Leu Cys	Ser Arg Leu Gln Asp Gln	
530	535	

<210> 78

<211> 2940

<212> DNA

<213> Homo sapiens

<400> 78

```

gccagctgtg ccggcggttg ttggetgccc tgcgcccggc cctccagcca gccttctgcc 60
ggccccgcgc cgatggaggt gccccagccg gagcccgccg caggctcggc tctcagtcca 120
gcaggcggtg gcggtggcgc ccagcgctcc ggccacctcc cgggcctcct gctgggatct 180
catggcctcc tggggtcccc ggtgcggggc gccgcttcct cgccggtcac caccctcacc 240
cagaccatgc acgacctcgc cgggctcggc agccgcagcc gcctgacgca cctatccctg 300
tctcgacggg catccgaatc ctccctgtcg tctgaatcct ccgaatcttc tgatgcaggt 360
ctctgcatgg attccccag ccctatggac ccccatatgg cggagcagac gtttgaacag 420
gccatccagg cagccagccg gatcattcga aacgagcagt ttgccatcag acgcttccag 480
tctatgcggc tgaggctgct gggccacagc cccgtgcttc ggaacatcac caactcccag 540
gcgcccgcgc gccggaggaa gagcgaggcg ggcagtggag ctgccagcag ctctggggaa 600
gacaaggaga atgatggatt tgtcttcaag atgccatgga agcccacaca tcccagctcc 660
acccatgctc tggcagagtg ggccagccgc aggggaagcct ttgccagag acccagctcg 720
ggccccgacc tgatgtgtct cagtcttgac cggaagatgg aagtggagga gctcagcccc 780
ctggccctag gtcgcttctc tctgacctc gcagaggggg atactgagga agatgatgga 840
tttgtggaca tcctagagag tgacttaaag gatgatgatg cagttcccc aggcatggag 900
agtctcatta gtgccccact ggtcaagacc ttggaaaagg aagaggaaaa ggacctcgtc 960
atgtacagca agtgccagcg gctcttccgc tctccgtcca tgccctgcag cgtgatccgg 1020

```

```

cccatcctca agaggctgga gcggccccag gacagggaca cgcccggtgca gaataagcgg 1080
aggcgaggcg tgacccctcc tgaggagcag caggaggctg aggaacctaa agcccgcgtc 1140
ctccgctcaa aatcactgtg tcacgatgag atcgagaacc tcctggacag tgaccaccga 1200
gagctgattg gagattactc taaggccttc ctctacaga cagtagacgg aaagcaccaa 1260
gacctcaagt acatctcacc agaaacgatg gtggccctat tgacgggcaa gttcagcaac 1320
atcgtggata agtttgtgat tgtagactgc agatacccct atgaatatga aggcgggcac 1380
atcaagactg cgggtgaactt gcccctggaa cgcgacgccc agagcttcct actgaagagc 1440
cccatcgcg cctgtagcct ggacaagaga gtcacctca ttttccactg tgaattctca 1500
tctgagcgtg ggccccgcat gtgccgtttc atcaggggaa gagaccgtgc tgtcaacgac 1560
taccacagcc tctactaccc tgagatgtat atcctgaaag gcggctacaa ggagttcttc 1620
cctcagcacc cgaacttctg tgaacccag gactaccggc ccatgaacca cgaggccttc 1680
aaggatgagc taaagacctt ccgctcaag actcgacgct gggctgggga gcggagccgg 1740
cgggagctct gtaccgggt gcaggaccag tgaggggcct gcgccagtc tgctacctcc 1800
cttgcccttc gaggcctgaa gccagctgcc ctatgggcct gccgggctga gggcctgctg 1860
gaggcctcag gtgctgtcca tgggaaagat ggtgtggtgt cctgcctgtc tgccccagcc 1920
cagattcccc tgtgtcatcc catcattttc catatcctgg tgccccccac ccctggaaga 1980
gcccagctctg ttgagttagt taagtgggt taataccagc ttaaaggcag tattttgtgt 2040
cctccaggag cttcttgttt ccttgtagg gttaaccctt catcttcctg tgcctgaaa 2100
cgctcctttg tgtgtgtgtc agctgaggct ggggagagcc gtggtccctg aggatgggtc 2160
agagctaaac tccttccctg cctgagagtc agctctctgc cctgtgtact tccggggcca 2220
gggctgcccc taatctctgt aggaaccgtg gtatgtctgc catgttgccc ctttctcttt 2280
tcccctttcc tgtcccacca tacgagcacc tccagcctga acagaagctc ttactctttc 2340
ctatttcagt gttacctgtg tgcttggtct gtttgacttt acgcccactc caggacactt 2400
ccgtagactg tttaggttcc cctgtcaa atcagttacc cactcggtcc cagttttgtt 2460
gccccagaaa gggatgttat tacccttggg ggtcccagg gcaagggtta aggcctgaat 2520
catgagcctg ctggaagccc agcccctact gctgtgaacc ctggggcctg actgctcaga 2580
acttgctgct gtcttgttgc ggatggatgg aaggttggat ggatgggtgg atggccgtgg 2640
atggccgtgg atgcgcagtg ccttgcatat ccaaaccagg tgggagcgtt ttgttgagca 2700
tgacacctgc agcaggaata tatgtgtgcc tatttgtgtg gacaaaaata tttacactta 2760
gggtttggag ctattcaaga ggaaatgtca cagaagcagc taaaccaagg actgagcacc 2820
ctctggattc tgaatctcaa gatgggggca ggcgtgtgct tgaaggccct gctgagtcac 2880
ctgttagggc cttggttcaa taaagcactg agcaagtga gaaaaaaaaa aaaaaaaaaa 2940

```

<210> 79

<211> 566

<212> PRT

<213> Homo sapiens

<400> 79

```

Met Glu Val Pro Gln Pro Glu Pro Ala Pro Gly Ser Ala Leu Ser Pro
1           5           10          15
Ala Gly Val Cys Gly Gly Ala Gln Arg Pro Gly His Leu Pro Gly Leu
20          25          30
Leu Leu Gly Ser His Gly Leu Leu Gly Ser Pro Val Arg Ala Ala Ala
35          40          45
Ser Ser Pro Val Thr Thr Leu Thr Gln Thr Met His Asp Leu Ala Gly
50          55          60
Leu Gly Ser Arg Ser Arg Leu Thr His Leu Ser Leu Ser Arg Arg Ala
65          70          75          80
Ser Glu Ser Ser Leu Ser Ser Glu Ser Ser Glu Ser Ser Asp Ala Gly
85          90          95
Leu Cys Met Asp Ser Pro Ser Pro Met Asp Pro His Met Ala Glu Gln
100         105         110
Thr Phe Glu Gln Ala Ile Gln Ala Ala Ser Arg Ile Ile Arg Asn Glu
115         120         125
Gln Phe Ala Ile Arg Arg Phe Gln Ser Met Pro Val Arg Leu Leu Gly
130         135         140

```


His Ser Pro Val Leu Arg Asn Ile Thr Asn Ser Gln Ala Pro Asp Gly
 145 150 155 160
 Arg Arg Lys Ser Glu Ala Gly Ser Gly Ala Ala Ser Ser Ser Gly Glu
 165 170 175
 Asp Lys Glu Asn Asp Gly Phe Val Phe Lys Met Pro Trp Lys Pro Thr
 180 185 190
 His Pro Ser Ser Thr His Ala Leu Ala Glu Trp Ala Ser Arg Arg Glu
 195 200 205
 Ala Phe Ala Gln Arg Pro Ser Ser Ala Pro Asp Leu Met Cys Leu Ser
 210 215 220
 Pro Asp Arg Lys Met Glu Val Glu Glu Leu Ser Pro Leu Ala Leu Gly
 225 230 235 240
 Arg Phe Ser Leu Thr Pro Ala Glu Gly Asp Thr Glu Glu Asp Asp Gly
 245 250 255
 Phe Val Asp Ile Leu Glu Ser Asp Leu Lys Asp Asp Asp Ala Val Pro
 260 265 270
 Pro Gly Met Glu Ser Leu Ile Ser Ala Pro Leu Val Lys Thr Leu Glu
 275 280 285
 Lys Glu Glu Glu Lys Asp Leu Val Met Tyr Ser Lys Cys Gln Arg Leu
 290 295 300
 Phe Arg Ser Pro Ser Met Pro Cys Ser Val Ile Arg Pro Ile Leu Lys
 305 310 315 320
 Arg Leu Glu Arg Pro Gln Asp Arg Asp Thr Pro Val Gln Asn Lys Arg
 325 330 335
 Arg Arg Ser Val Thr Pro Pro Glu Glu Gln Gln Glu Ala Glu Glu Pro
 340 345 350
 Lys Ala Arg Val Leu Arg Ser Lys Ser Leu Cys His Asp Glu Ile Glu
 355 360 365
 Asn Leu Leu Asp Ser Asp His Arg Glu Leu Ile Gly Asp Tyr Ser Lys
 370 375 380
 Ala Phe Leu Leu Gln Thr Val Asp Gly Lys His Gln Asp Leu Lys Tyr
 385 390 395 400
 Ile Ser Pro Glu Thr Met Val Ala Leu Leu Thr Gly Lys Phe Ser Asn
 405 410 415
 Ile Val Asp Lys Phe Val Ile Val Asp Cys Arg Tyr Pro Tyr Glu Tyr
 420 425 430
 Glu Gly Gly His Ile Lys Thr Ala Val Asn Leu Pro Leu Glu Arg Asp
 435 440 445
 Ala Glu Ser Phe Leu Leu Lys Ser Pro Ile Ala Pro Cys Ser Leu Asp
 450 455 460
 Lys Arg Val Ile Leu Ile Phe His Cys Glu Phe Ser Ser Glu Arg Gly
 465 470 475 480
 Pro Arg Met Cys Arg Phe Ile Arg Glu Arg Asp Arg Ala Val Asn Asp
 485 490 495
 Tyr Pro Ser Leu Tyr Tyr Pro Glu Met Tyr Ile Leu Lys Gly Gly Tyr
 500 505 510
 Lys Glu Phe Phe Pro Gln His Pro Asn Phe Cys Glu Pro Gln Asp Tyr
 515 520 525
 Arg Pro Met Asn His Glu Ala Phe Lys Asp Glu Leu Lys Thr Phe Arg
 530 535 540
 Leu Lys Thr Arg Ser Trp Ala Gly Glu Arg Ser Arg Arg Glu Leu Cys
 545 550 555 560
 Ser Arg Leu Gln Asp Gln
 565

<210> 80

<211> 2115

<212> DNA
<213> Homo sapiens

<400> 80

```

ggtcaacgcc tgcggctggt gatattcttg ctcagaggcc gtaacttttg ccttctgctc 60
aggggaagact ctgagtcgga cgttggccta cccagtcgga aggcagagct gcaatctagt 120
taactacctc ctttcccta gatttccctt cattctgctc aagtcttcgc ctgtgtccga 180
tcctatctta ctttctctcc tcttgtagca agcctcagac tccaggcttg agctagggtt 240
tgtttttctc ctggtgagaa ttcgaagacc atgtctacgg aactcttctc atccacaaga 300
gaggaaggaa gctctggctc aggaccaggt tttagggtcta atcaaaggaa aatgttaaag 360
ctgctcctgg agagagacac ttcctttacc gtctgtccag atgtccctag aactccagtg 420
ggcaaatttc ttggtgattc tgcaaaccta agcattttgt ctggaggaa cccaaaatgt 480
tgctctgata tttcgaatct tagcagtggt gagataactg ccaactcagct taccacttct 540
gcagaccttg atgaaactgg tcacctggat tcttcaggac ttcaggaagt gcatttagct 600
gggatgaatc atgaccagca cctaataaaa tgtagcccag cacagcttct ttgtagcact 660
ccgaatgggt tggacgtgg ccatagaag agagatgcaa tgtgtagtct atctgcaaat 720
aaagaaaatg acaatggaaa cttggtggac agtgaaatga aatatttggg cagtccatt 780
actactgttc caaaattgga taaaaatcca aacctaggag aagaccaggc agaagagatt 840
tcagatgaat taatggagtt tccctgaaa gatcaagaag caaagggtgag cagaagtggc 900
ctatatcgct ccccgctgat gccagagaac ttgaacaggc caagactgaa gcaggtggaa 960
aaattcaagg acaacacaat accagataaa gttaaaaaaa agtatttttc tggccaagga 1020
aagctcagga agggcttatg tttaaagaag acagtctctc tgtgtgacat tactatcact 1080
cagatgctgg aggaagattc taaccagggg cacctgattg gtgatttttc caaggatgt 1140
gcgctgcaa cctgtgcagg gaaacaccaa gatctgaagt atgtcaacc agaaacagtg 1200
gctgccttac tgcggggaa gttccagggt ctgattgaga agttttatgt cattgattgt 1260
cgctatccat atgagtatct gggaggacac atccaggagg ccttaaaact atatagtcag 1320
gaagaactgt ttaacttctt tctgaagaag cccatcgtcc ctttggacac ccagaagaga 1380
ataatcatcg tgttccactg tgaattctcc tcagagagg gccccgaat gtgccgctgt 1440
ctgcgtgaag aggacagggt tctgaaccag tatcctgcat tgtactacc agagctatat 1500
atccttaaag gcggtacag agacttcttt ccagaatata tggaaactgt tgaaccacag 1560
agctactgcc ctatgcatca tcaggaccac aagactgagt tgctgagggt tcgaagccag 1620
agcaaagtgc aggaagggga gcggcagctg cgggagcaga ttgcccttct ggtgaaggac 1680
atgagcccat gataacattc cagccactgg ctgctaacaa gtcacaaaa agacactgca 1740
gaaaccctga gcagaaagag gccttctgga tggccaaacc caagattatt aaaagatgtc 1800
tctgcaaaac aacaggctac caacttgat ccaggcctgg gaatggatta ggtttcagca 1860
gagctgaaag ctggtggcag agtcctggag ctggctctat aaggcagcct tgagttgcat 1920
agagatttgt attggttcag ggaactctgg cattcctttt cccaactcct catgtcttct 1980
cacaagccag ccaactcttt ctctctgggc ttccggctat gcaagagcgt tgtctacct 2040
ctttctttgt attttcttc tttgtttccc cctctttctt ttttaaaaat gaaaaataa 2100
aactacaga atgag                                     2115

```

<210> 81
<211> 473
<212> PRT
<213> Homo sapiens

<400> 81

```

Met Ser Thr Glu Leu Phe Ser Ser Thr Arg Glu Glu Gly Ser Ser Gly
 1           5           10           15
Ser Gly Pro Ser Phe Arg Ser Asn Gln Arg Lys Met Leu Asn Leu Leu
 20           25           30
Leu Glu Arg Asp Thr Ser Phe Thr Val Cys Pro Asp Val Pro Arg Thr
 35           40           45
Pro Val Gly Lys Phe Leu Gly Asp Ser Ala Asn Leu Ser Ile Leu Ser
 50           55           60
Gly Gly Thr Pro Lys Cys Cys Leu Asp Leu Ser Asn Leu Ser Ser Gly
 65           70           75           80
Glu Ile Thr Ala Thr Gln Leu Thr Thr Ser Ala Asp Leu Asp Glu Thr

```

				85					90					95	
Gly	His	Leu	Asp	Ser	Ser	Gly	Leu	Gln	Glu	Val	His	Leu	Ala	Gly	Met
			100					105					110		
Asn	His	Asp	Gln	His	Leu	Met	Lys	Cys	Ser	Pro	Ala	Gln	Leu	Leu	Cys
		115					120					125			
Ser	Thr	Pro	Asn	Gly	Leu	Asp	Arg	Gly	His	Arg	Lys	Arg	Asp	Ala	Met
	130					135					140				
Cys	Ser	Ser	Ser	Ala	Asn	Lys	Glu	Asn	Asp	Asn	Gly	Asn	Leu	Val	Asp
145					150				155						160
Ser	Glu	Met	Lys	Tyr	Leu	Gly	Ser	Pro	Ile	Thr	Thr	Val	Pro	Lys	Leu
			165						170					175	
Asp	Lys	Asn	Pro	Asn	Leu	Gly	Glu	Asp	Gln	Ala	Glu	Glu	Ile	Ser	Asp
			180					185					190		
Glu	Leu	Met	Glu	Phe	Ser	Leu	Lys	Asp	Gln	Glu	Ala	Lys	Val	Ser	Arg
		195					200					205			
Ser	Gly	Leu	Tyr	Arg	Ser	Pro	Ser	Met	Pro	Glu	Asn	Leu	Asn	Arg	Pro
	210					215					220				
Arg	Leu	Lys	Gln	Val	Glu	Lys	Phe	Lys	Asp	Asn	Thr	Ile	Pro	Asp	Lys
225					230				235						240
Val	Lys	Lys	Lys	Tyr	Phe	Ser	Gly	Gln	Gly	Lys	Leu	Arg	Lys	Gly	Leu
			245						250					255	
Cys	Leu	Lys	Lys	Thr	Val	Ser	Leu	Cys	Asp	Ile	Thr	Ile	Thr	Gln	Met
			260					265					270		
Leu	Glu	Glu	Asp	Ser	Asn	Gln	Gly	His	Leu	Ile	Gly	Asp	Phe	Ser	Lys
		275					280					285			
Val	Cys	Ala	Leu	Pro	Thr	Val	Ser	Gly	Lys	His	Gln	Asp	Leu	Lys	Tyr
	290					295					300				
Val	Asn	Pro	Glu	Thr	Val	Ala	Ala	Leu	Leu	Ser	Gly	Lys	Phe	Gln	Gly
305					310					315					320
Leu	Ile	Glu	Lys	Phe	Tyr	Val	Ile	Asp	Cys	Arg	Tyr	Pro	Tyr	Glu	Tyr
			325						330					335	
Leu	Gly	Gly	His	Ile	Gln	Gly	Ala	Leu	Asn	Leu	Tyr	Ser	Gln	Glu	Glu
			340					345					350		
Leu	Phe	Asn	Phe	Phe	Leu	Lys	Lys	Pro	Ile	Val	Pro	Leu	Asp	Thr	Gln
		355					360					365			
Lys	Arg	Ile	Ile	Ile	Val	Phe	His	Cys	Glu	Phe	Ser	Ser	Glu	Arg	Gly
	370					375					380				
Pro	Arg	Met	Cys	Arg	Cys	Leu	Arg	Glu	Glu	Asp	Arg	Ser	Leu	Asn	Gln
385					390					395					400
Tyr	Pro	Ala	Leu	Tyr	Tyr	Pro	Glu	Leu	Tyr	Ile	Leu	Lys	Gly	Gly	Tyr
				405					410					415	
Arg	Asp	Phe	Phe	Pro	Glu	Tyr	Met	Glu	Leu	Cys	Glu	Pro	Gln	Ser	Tyr
			420					425					430		
Cys	Pro	Met	His	His	Gln	Asp	His	Lys	Thr	Glu	Leu	Leu	Arg	C	

<210> 82

<211> 1896

<212> DNA

<213> Homo sapiens

<400> 82

ggccaacgcc tgcggctggt gatattcttg ctcagaggcc gtaactttgg ccttctgctc 60

```

aggggaagact ctgagtcgga cgttggccta cccagtcgga aggcagagct gcaatctagt 120
taactacctc ctttccccta gatttccttt cattctgctc aagtcttcgc ctgtgtccga 180
tccctatcta ctttctctcc tctttagaca agcctcagac tccaggcttg agctagggtt 240
tgtttttctc ctggtgagaa ttcaagacc atgtctacgg aactcttctc atccacaaga 300
gaggaaggaa gctctggctc aggaccagt tttaggctta atcaaaggaa aatgttaaag 360
ctgctcctgg agagagacac ttccctttacc gtctgtccag atgtccctag aactccagt 420
ggcaaatttc ttggtgattc tgcaaacctc agcattttgt ctgggtcacc tggattcttc 480
aggacttcag gaagtgcatt tagctgggat gacaatggaa acttggtgga cagtgaaatg 540
aaatatttgg gcagtcctat tactactgtt ccaaaattgg ataaaaatcc aaacctagga 600
gaagaccagg cagaagagat ttcagatgaa ttaattggagt tttccctgaa agatcaagaa 660
gcaaagggtg gcagaagtgg cctatatcgc tccccgtcga tgccagagaa cttgaacagg 720
ccaagactga agcaggtgga aaaattcaag gacaacacaa taccagataa agttaaaaaa 780
aagtattttt ctggccaagg aaagctcagg aagggttat gtttaaagaa gacagtctct 840
ctgtgtgaca ttactatcac tcagatgctg gaggaagatt ctaaccaggg gcacctgatt 900
ggtgattttt ccaaggtatg tgcgctgcca accgtgtcag ggaaacacca agatctgaag 960
tatgtcaacc cagaaacagt ggctgcctta ctgtcgggga agttccaggg tctgattgag 1020
aagttttatg tcattgattg tcgctatcca tatgagtatc tgggaggaca catccaggga 1080
gccttaaaat tatatagtca ggaagaactg ttttaacttct ttctgaagaa gcccatcgtc 1140
cctttggaca cccagaagag aataatcatc gtgttccact gtgaattctc ctcagagagg 1200
ggcccccgaa tgtgccgctg tctgcgtgaa gaggacagg ctctgaacca gtatcctgca 1260
ttgtactacc cagagctata tatccttaaa ggccgctaca gagacttctt tccagaatat 1320
atggaactgt gtgaaccaca gagctactgc cctatgcata atcaggacca caagactgag 1380
ttgctgaggt gtcgaagcca gagcaaagtg caggaagggg agcggcagct gcgggagcag 1440
attgcccttc tgggtgaagga catgagccca tgataacatt ccagccactg gctgctaaca 1500
agtcaccaa aagacactgc agaaaccctg agcagaaaga ggccttctgg atggccaaac 1560
ccaagattat taaaagatgt ctctgcaaac caacaggcta ccaacttgta tccaggcctg 1620
ggaatggatt aggtttcagc agagctgaaa gctgggtggc gagtcctgga gctggctcta 1680
taaggcagcc ttgagttgca tagagatttg tattgggttca gggaactctg gcattccttt 1740
tcccaactcc tcatgtcttc tcacaagcca gccaaactct tctctctggg cttcgggcta 1800
tgcaagagcg ttgtctacct tctttctttg tattttcctt ctttgtttcc ccctctttct 1860
tttttaaaaa tggaaaaata aacactacag aatgag 1896

```

<210> 83

<211> 400

<212> PRT

<213> Homo sapiens

<400> 83

```

Met Ser Thr Glu Leu Phe Ser Ser Thr Arg Glu Glu Gly Ser Ser Gly
 1           5           10           15
Ser Gly Pro Ser Phe Arg Ser Asn Gln Arg Lys Met Leu Asn Leu Leu
          20           25           30
Leu Glu Arg Asp Thr Ser Phe Thr Val Cys Pro Asp Val Pro Arg Thr
          35           40           45
Pro Val Gly Lys Phe Leu Gly Asp Ser Ala Asn Leu Ser Ile Leu Ser
          50           55           60
Gly Ser Pro Gly Phe Phe Arg Thr Ser Gly Ser Ala Phe Ser Trp Asp
65           70           75           80
Asp Asn Gly Asn Leu Val Asp Ser Glu Met Lys Tyr Leu Gly Ser Pro
          85           90           95
Ile Thr Thr Val Pro Lys Leu Asp Lys Asn Pro Asn Leu Gly Glu Asp
          100          105          110
Gln Ala Glu Glu Ile Ser Asp Glu Leu Met Glu Phe Ser Leu Lys Asp
          115          120          125
Gln Glu Ala Lys Val Ser Arg Ser Gly Leu Tyr Arg Ser Pro Ser Met
          130          135          140
Pro Glu Asn Leu Asn Arg Pro Arg Leu Lys Gln Val Glu Lys Phe Lys
145          150          155          160

```

Asp Asn Thr Ile Pro Asp Lys Val Lys Lys Lys Tyr Phe Ser Gly Gln
 165 170 175
 Gly Lys Leu Arg Lys Gly Leu Cys Leu Lys Lys Thr Val Ser Leu Cys
 180 185 190
 Asp Ile Thr Ile Thr Gln Met Leu Glu Glu Asp Ser Asn Gln Gly His
 195 200 205
 Leu Ile Gly Asp Phe Ser Lys Val Cys Ala Leu Pro Thr Val Ser Gly
 210 215 220
 Lys His Gln Asp Leu Lys Tyr Val Asn Pro Glu Thr Val Ala Ala Leu
 225 230 235 240
 Leu Ser Gly Lys Phe Gln Gly Leu Ile Glu Lys Phe Tyr Val Ile Asp
 245 250 255
 Cys Arg Tyr Pro Tyr Glu Tyr Leu Gly Gly His Ile Gln Gly Ala Leu
 260 265 270
 Asn Leu Tyr Ser Gln Glu Glu Leu Phe Asn Phe Phe Leu Lys Lys Pro
 275 280 285
 Ile Val Pro Leu Asp Thr Gln Lys Arg Ile Ile Ile Val Phe His Cys
 290 295 300
 Glu Phe Ser Ser Glu Arg Gly Pro Arg Met Cys Arg Cys Leu Arg Glu
 305 310 315 320
 Glu Asp Arg Ser Leu Asn Gln Tyr Pro Ala Leu Tyr Tyr Pro Glu Leu
 325 330 335
 Tyr Ile Leu Lys Gly Gly Tyr Arg Asp Phe Phe Pro Glu Tyr Met Glu
 340 345 350
 Leu Cys Glu Pro Gln Ser Tyr Cys Pro Met His His Gln Asp His Lys
 355 360 365
 Thr Glu Leu Leu Arg Cys Arg Ser Gln Ser Lys Val Gln Glu Gly Glu
 370 375 380
 Arg Gln Leu Arg Glu Gln Ile Ala Leu Leu Val Lys Asp Met Ser Pro
 385 390 395 400

<210> 84

<211> 1785

<212> DNA

<213> Homo sapiens

<400> 84

atggcagcgg agtcagggga actaatcggg gcttgtgagt tcatgaaaga tcggttatat 60
 tttgctactt taaggaatag accaaaaagc acagtaaata ccactatatt ctccatcgat 120
 gaggagctgg tctatgaaaa tttctatgca gatttttgac cgctgaactt ggcaatgggtg 180
 tacagatatt gctgcaaact aaacaagaaa ctaaaatcat acagtttgtc aagaaagaaa 240
 atagtgcact acacctgttt tgaccaacgg aaaagagcaa atgcagcatt tttgataggt 300
 gcctatgcag taatctatatt aaagaagaca ccagaagaag cctacagagc actcctgtct 360
 ggctcaaacc cccctatct tccattcagg gatgcttcct ttggaaattg cacttacaat 420
 ctcaccattc tcgactgttt gcaggggaatc agaaagggat tacaacatgg attttttgac 480
 tttgagacat ttgatgtgga tgaatatgaa cattatgagc gagttgaaaa tgggtgacttc 540
 aactggattg ttccaggaaa attttttagca tttagtggac cacatcctaa aagcaaaatt 600
 gagaatgggt atcctcttca cgccctgaa gcctactttc cttatttcaa aaagcataat 660
 gtgactgcag ttgtgaggct aaacaaaaag atttatgagg caaagcgctt cacagacgct 720
 ggcttcgagc actatgacct cttcttcata gatggcagca caccagtgca caacatcgtg 780
 cgaagggtcc tgaacatctg tgagaacacc gaaggggcca tcgccgttca ctgcaaagct 840
 ggtcttgaaa gaacaggagc attgatagcc tgttatgtaa tgaaacacta cagggtttaca 900
 catgctgaaa taattgcttg gattagaata tgccggccag gctctattat aggacccag 960
 cagcacttcc tggaagaaaa acaagcatcg ttgtgggtcc aaggagacat tttccgatcc 1020
 aaactgaaaa atcgaccatc cagtgaagga agtattaata aaattctttc tggcctagat 1080
 gatatgtcta ttggtggaaa tctttcaaaa acacaaaaca tggaacgatt tggagaggat 1140
 aacttagaag atgatgatgt ggaaatgaaa aatggtataa ccaggggaga caaactacgt 1200

```

gccttaaaaa gtcagagaca gccacgtacc tcaccatcct gtgcatttag gtcagatgat 1260
acaaaaggac atccaagagc agtgtcccag cctttcagat taagttcatc cctgcaagga 1320
tctgcagtta ctttgaagac atcaaaaatg gcactgtccc cttcagcaac ggccaagagg 1380
atcaacagaa cttctttgtc ttccgggtgcc actgtaagaa gcttttccat aaactcccgg 1440
ctagccagtt ctctagggaa cttgaatgct gcaacagatg atccagagaa caaaaagacc 1500
tcctcatcct ctaaggcagg cttcacagcc agcccgttta ccaacctctt gaatggcagc 1560
tcccagccaa ctaccagaaa ttaccctgag ctcaacaata atcagtacaa cagaagcagc 1620
aacagcaacg ggggcaacct gaacagcccc ccaggccccc acagcgccaa gacagaggag 1680
cacaccacca tcctccgacc ctctacacc gggctttctt cttcttcagc gagattcctg 1740
agccgttcta tcccttcctt tcagtctgaa tatgttcatt actaa 1785

```

<210> 85

<211> 594

<212> PRT

<213> Homo sapiens

<400> 85

```

Met Ala Ala Glu Ser Gly Glu Leu Ile Gly Ala Cys Glu Phe Met Lys
 1           5           10           15
Asp Arg Leu Tyr Phe Ala Thr Leu Arg Asn Arg Pro Lys Ser Thr Val
      20           25           30
Asn Thr His Tyr Phe Ser Ile Asp Glu Glu Leu Val Tyr Glu Asn Phe
      35           40           45
Tyr Ala Asp Phe Gly Pro Leu Asn Leu Ala Met Val Tyr Arg Tyr Cys
      50           55           60
Cys Lys Leu Asn Lys Lys Leu Lys Ser Tyr Ser Leu Ser Arg Lys Lys
      65           70           75           80
Ile Val His Tyr Thr Cys Phe Asp Gln Arg Lys Arg Ala Asn Ala Ala
      85           90           95
Phe Leu Ile Gly Ala Tyr Ala Val Ile Tyr Leu Lys Lys Thr Pro Glu
      100          105          110
Glu Ala Tyr Arg Ala Leu Leu Ser Gly Ser Asn Pro Pro Tyr Leu Pro
      115          120          125
Phe Arg Asp Ala Ser Phe Gly Asn Cys Thr Tyr Asn Leu Thr Ile Leu
      130          135          140
Asp Cys Leu Gln Gly Ile Arg Lys Gly Leu Gln His Gly Phe Phe Asp
      145          150          155          160
Phe Glu Thr Phe Asp Val Asp Glu Tyr Glu His Tyr Glu Arg Val Glu
      165          170          175
Asn Gly Asp Phe Asn Trp Ile Val Pro Gly Lys Phe Leu Ala Phe Ser
      180          185          190
Gly Pro His Pro Lys Ser Lys Ile Glu Asn Gly Tyr Pro Leu His Ala
      195          200          205
Pro Glu Ala Tyr Phe Pro Tyr Phe Lys Lys His Asn Val Thr Ala Val
      210          215          220
Val Arg Leu Asn Lys Lys Ile Tyr Glu Ala Lys Arg Phe Thr Asp Ala
      225          230          235          240
Gly Phe Glu His Tyr Asp Leu Phe Phe Ile Asp Gly Ser Thr Pro Ser
      245          250          255
Asp Asn Ile Val Arg Arg Phe Leu Asn Ile Cys Glu Asn Thr Glu Gly
      260          265          270
Ala Ile Ala Val His Cys Lys Ala Gly Leu Gly Arg Thr Gly Thr Leu
      275          280          285
Ile Ala Cys Tyr Val Met Lys His Tyr Arg Phe Thr His Ala Glu Ile
      290          295          300
Ile Ala Trp Ile Arg Ile Cys Arg Pro Gly Ser Ile Ile Gly Pro Gln
      305          310          315          320
Gln His Phe Leu Glu Glu Lys Gln Ala Ser Leu Trp Val Gln Gly Asp

```

[illegible]

```
<210> 86
<211> 2438
<212> DNA
<213> Homo sapiens
```

<400>	86						
cgaagaggat	ccggagcagc	tgctgccagc	ccgcgggcac	tgaagtcttc	ccggctgccg	60	
ctcgagtagc	cacgggcgcg	atcgggacca	gaagtctcct	cctccatgat	cactttggaa	120	
gccgggggaa	gactttgcc	tgccctgaga	gctggtctgc	gtttcccagg	cgcggcggcg	180	
gcggagcagc	agctgcagca	gccgagtgca	aataggagcg	gccacagcca	ggggcggtgtg	240	
cgccccgcgc	ggagcgaagt	cgggttcccc	tcggaatgtc	cccggggcgc	ccggcgcgct	300	
gaccccgaa	ccgcctccgc	cttcggcgcc	tgctgcctcc	ctcggccagg	cttggtgttc	360	
gggactgtga	gcttcctggc	tcctgggcag	tggggaagcc	cccgggggcg	agtgacctca	420	
gctggccacg	accagacct	cccccgtcgc	tatctcgctt	aagatggcag	cggagtcagg	480	
ggaactaatc	ggggcttgtg	agttcatgaa	agatcggtta	tattttgcta	ctttaaggaa	540	
tagacacaaa	agcagagtaa	ataccacta	tttctccatc	gatgaggagc	tggtctatga	600	
aaatttctat	gcagattttg	gaccgcgtgaa	cttggcaatg	gtgtacagat	attgctgcaa	660	
actaacaacg	aaactaaaat	catacagttt	gtcaagaaag	aaaatagtgc	actaacctg	720	
ttttgaccaa	cggaaaagag	caaatgcagc	atttttgata	ggtgcctatg	cagtaactca	780	
tttaaagaag	acaccagaag	aagcctacag	agcactcctg	ttcggctcaa	accccccta	840	
tcttccattc	agggatgctt	cctttggaaa	ttgcacttac	aatctcacca	ttctcgactg	900	

```

tttgcagggga atcagaaagg gattacaaca tggatttttt gactttgaga catttgatgt 960
ggatgaatat gaacattatg agcgagttga aaatggtgac ttcaactgga ttgttccagg 1020
aaaatttttta gcatttagtg gaccacatcc taaaagcaaa attgagaatg gttatcctct 1080
tcacgccccct gaagcctact ttccttattt caaaaagcat aatgtgactg cagttgtgag 1140
gctaaacaaa aagatttatg aggcaaagcg cttcacagac gctggcttcg agcactatga 1200
cctcttcttc atagatggca gcacaccag tgacaacatc gtgcgaagggt tcctgaacat 1260
ctgtgagaac accgaagggg ccatcgccgt tcaactgcaa gctggtcttg gaagaacagg 1320
gacattgata gcctgttatg taatgaaaca ctacaggttt acacatgctg aaataattgc 1380
ttggattaga atatgccggc caggctctat tataggaccc cagcagcact tcctggaaga 1440
aaaacaagca tcgttgtggg tccaaggaga ctttttccga tccaaactga aaaatcgacc 1500
atccagtga ggaagtatta ataaaattct ttctggccta gatgatatgt ctattggtgg 1560
aaatctttca aaaacacaaa acatggaacg atttgagag gataacttag aagatgatga 1620
tgtggaaatg aaaaatggtg taaccaggg agacaaacta cgtgccttaa aaagtcagag 1680
acagccacgt acctcaccat cctgtgcatt taggtcagat gatacaaaaag gacatccaag 1740
agcagtgtcc cagcctttca gattaagttc atccctgcaa ggatctgcag ttactttgaa 1800
gacatcaaaa atggcactgt ccccttcagc aacggccaag aggatcaaca gaacttcttt 1860
gtcttcgggt gccactgtaa gaagcttttc cataaactcc cggctagcca gttctctagg 1920
gaacttgaat gctgcaacag atgatccaga gaacaaaaag acctcctcat cctctaaggc 1980
aggcttcaca gccagcccgt ttaccaacct ctggaatggc agctcccagc caactaccag 2040
aaattacctt gagctcaaca ataatcagta caacagaagc agcaacagca acggggggcaa 2100
cctgaacagc cccccaggcc cccacagcgc caagacagag gagcacacca ccatectccg 2160
accctcctac accgggcttt cttcttcttc agcgagattc ctgagccgtt ctatccctgt 2220
aagtgcgcag acaccacctc ctggtcctca gaacctgaa tgcaacttct gtgccttgcc 2280
ttcccagccg aggctgccac caaagaaatt taatagtgcc aaggaagcct tctgagcgat 2340
gccttccttc tgtgtgtgta aactgtctat gcactacatt ctgctagctc ctcttcaagt 2400
aaacgccaag tcacaaaaaa aaaaaaaaaa aaaaaaaa 2438

```

<210> 87

<211> 623

<212> PRT

<213> Homo sapiens

<400> 87

```

Met Ala Ala Glu Ser Gly Glu Leu Ile Gly Ala Cys Glu Phe Met Lys
1          5          10          15
Asp Arg Leu Tyr Phe Ala Thr Leu Arg Asn Arg Pro Lys Ser Thr Val
20        25        30
Asn Thr His Tyr Phe Ser Ile Asp Glu Glu Leu Val Tyr Glu Asn Phe
35        40        45
Tyr Ala Asp Phe Gly Pro Leu Asn Leu Ala Met Val Tyr Arg Tyr Cys
50        55        60
Cys Lys Leu Asn Lys Lys Leu Lys Ser Tyr Ser Leu Ser Arg Lys Lys
65        70        75        80
Ile Val His Tyr Thr Cys Phe Asp Gln Arg Lys Arg Ala Asn Ala Ala
85        90        95
Phe Leu Ile Gly Ala Tyr Ala Val Ile Tyr Leu Lys Lys Thr Pro Glu
100       105       110
Glu Ala Tyr Arg Ala Leu Leu Ser Gly Ser Asn Pro Pro Tyr Leu Pro
115       120       125
Phe Arg Asp Ala Ser Phe Gly Asn Cys Thr Tyr Asn Leu Thr Ile Leu
130       135       140
Asp Cys Leu Gln Gly Ile Arg Lys Gly Leu Gln His Gly Phe Phe Asp
145       150       155       160
Phe Glu Thr Phe Asp Val Asp Glu Tyr Glu His Tyr Glu Arg Val Glu
165       170       175
Asn Gly Asp Phe Asn Trp Ile Val Pro Gly Lys Phe Leu Ala Phe Ser
180       185       190
Gly Pro His Pro Lys Ser Lys Ile Glu Asn Gly Tyr Pro Leu His Ala

```


195	200	205
Pro Glu Ala Tyr Phe Pro Tyr Phe Lys Lys His Asn Val Thr Ala Val		
210	215	220
Val Arg Leu Asn Lys Lys Ile Tyr Glu Ala Lys Arg Phe Thr Asp Ala		
225	230	235
Gly Phe Glu His Tyr Asp Leu Phe Phe Ile Asp Gly Ser Thr Pro Ser		
245	250	255
Asp Asn Ile Val Arg Arg Phe Leu Asn Ile Cys Glu Asn Thr Glu Gly		
260	265	270
Ala Ile Ala Val His Cys Lys Ala Gly Leu Gly Arg Thr Gly Thr Leu		
275	280	285
Ile Ala Cys Tyr Val Met Lys His Tyr Arg Phe Thr His Ala Glu Ile		
290	295	300
Ile Ala Trp Ile Arg Ile Cys Arg Pro Gly Ser Ile Ile Gly Pro Gln		
305	310	315
Gln His Phe Leu Glu Lys Gln Ala Ser Leu Trp Val Gln Gly Asp		
325	330	335
Ile Phe Arg Ser Lys Leu Lys Asn Arg Pro Ser Ser Glu Gly Ser Ile		
340	345	350
Asn Lys Ile Leu Ser Gly Leu Asp Asp Met Ser Ile Gly Gly Asn Leu		
355	360	365
Ser Lys Thr Gln Asn Met Glu Arg Phe Gly Glu Asp Asn Leu Glu Asp		
370	375	380
Asp Asp Val Glu Met Lys Asn Gly Ile Thr Gln Gly Asp Lys Leu Arg		
385	390	395
Ala Leu Lys Ser Gln Arg Gln Pro Arg Thr Ser Pro Ser Cys Ala Phe		
405	410	415
Arg Ser Asp Asp Thr Lys Gly His Pro Arg Ala Val Ser Gln Pro Phe		
420	425	430
Arg Leu Ser Ser Ser Leu Gln Gly Ser Ala Val Thr Leu Lys Thr Ser		
435	440	445
Lys Met Ala Leu Ser Pro Ser Ala Thr Ala Lys Arg Ile Asn Arg Thr		
450	455	460
Ser Leu Ser Ser Gly Ala Thr Val Arg Ser Phe Ser Ile Asn Ser Arg		
465	470	475
Leu Ala Ser Ser Leu Gly Asn Leu Asn Ala Ala Thr Asp Asp Pro Glu		
485	490	495
Asn Lys Lys Thr Ser Ser Ser Ser Lys Ala Gly Phe Thr Ala Ser Pro		
500	505	510
Phe Thr Asn Leu Leu Asn Gly Ser Ser Gln Pro Thr Thr Arg Asn Tyr		
515	520	525
Pro Glu Leu Asn Asn Asn Gln Tyr Asn Arg Ser Ser Asn Ser Asn Gly		
530	535	540
Gly Asn Leu Asn Ser Pro Pro Gly Pro His Ser Ala Lys Thr Glu Glu		
545	550	555
His Thr Thr Ile Leu Arg Pro Ser Tyr Thr Gly Leu Ser Ser Ser Ser		
565	570	575
Ala Arg Phe Leu Ser Arg Ser Ile Pro Val Ser Ala Gln Thr Pro Pro		
580	585	590
Pro Gly Pro Gln Asn Pro Glu Cys Asn Phe Cys Ala Leu Pro Ser Gln		
595	600	605
Pro Arg Leu Pro Pro Lys Lys Phe Asn Ser Ala Lys Glu Ala Phe		
610	615	620

<210> 88

<211> 1890

<212> DNA

<213> Homo sapiens

<400> 88

```

ccggagcagc  tgctgccagc  ccgcggggcac  tgaagtcctc  ccggctgccg  ctcgagtagc  60
cacggggcgcg  atcggggacca  gaagtctcct  cctccatgat  cactttggaa  gccgggggaa  120
gactttgccc  tgccctgaga  gctggtctgc  gtttcccagg  cgcggcggcg  gcggagcagc  180
agctgcagca  gccgagtcga  aataggagcg  gccacagcca  ggggcgtgtg  cgccccgcgc  240
ggagcgagct  cgggttcccc  tcggaatgtc  cccggggcgc  ccggcgcgct  gaccccgaa  300
ccgcctccgc  cttcggcgcc  tgctgcctcc  ctcgccagg  cttgttggtc  gggactgtga  360
gcttctctgg  tcctgggcag  tggggaagcc  cccgggggcg  agtgacctca  gctggccacg  420
accagccct  ccccgctgcg  tatctcgctt  aagatggcag  cggagtcagg  ggaactaatc  480
ggggcttgtg  agttcatgaa  agatcgggta  tattttgcta  ctttaaggaa  tagacaaaaa  540
agcacagtaa  atacccacta  tttctccatc  gatgaggagc  tggctctatg  aaatttctat  600
gcagattttg  gaccgctgaa  ctgggcaatg  gtgtacagat  attgctgcaa  actaaacaag  660
aaactaaaat  catacagttt  gtcaagaaag  aaaatagtgc  actacacctg  ttttgaccaa  720
cggaaaagag  caaatgcagc  atttttgata  ggtgcctatg  cagtaatcta  ttttaagaag  780
acaccagaag  aagcctacag  agcactcctg  tctggctcaa  accccccta  tcttccattc  840
agggatgctt  cctttggaaa  ttgcacttac  aatctcacca  ttctcgactg  tttgcaggga  900
atcagaaaag  gattacaaca  tggatttttt  gactttgaga  catttgatgt  ggatgaatat  960
gaacattatg  agcgagtga  aaatggtgac  ttcaactgga  ttgttccagg  aaaattttta  1020
gcatttagtg  gaccacatcc  taaaagcaaa  attgagaatg  gttatcctct  tcacgcccc  1080
gaagcctact  ttccttattt  caaaaagcat  aatgtgactg  cagttgtgag  gctaaacaaa  1140
aagatttatg  aggcaaacg  cttcacagac  gctggcttcg  agcactatga  cctcttcttc  1200
atagatggca  gcacaccag  tgacaacatc  gtgcgaaggt  tcctgaacat  ctgtgagaac  1260
accgaagggg  ccacgcctg  tcaactgcaa  gctggtcttg  gaagaacagg  gacattgata  1320
gcctgttatg  taatgaaaca  ctacagggtt  acacatgctg  aaataattgc  ttggattaga  1380
atatgccggc  caggctctat  tataggacc  cagcagcact  tcctggaaga  aaaacaagca  1440
tcgttgtggg  tccaaggaga  cattttccga  tccaaactga  aaaatcgacc  atccagtga  1500
ggaagtatta  ataaaattct  ttctggccta  gatgatatgt  ctattggtgg  aaatctttca  1560
aaaacacaaa  acatggaacg  atttgagag  gtaagttttc  ctaggagat  tctatcttct  1620
taaaactgat  gttctgcatt  tgtttctcag  ttggacctat  ataacatagc  agtgtctttt  1680
ctctggatgc  cagcagtagc  aagtttttag  aagtagagcc  atccgtctat  atagcaagaa  1740
gcagaggaaa  gaaaccaatt  gcccttaaaa  aaaaaaagct  ataatttaag  gagtaaat  1800
taaaggaggc  tactctggta  aggggtaata  tttatagaaa  ggaaacagaa  aagcaaactt  1860
tctatttgaa  aaaaaaaaaa  aaaaaaaaaa  1890

```

<210> 89

<211> 383

<212> PRT

<213> Homo sapiens

<400> 89

```

Met Ala Ala Glu Ser Gly Glu Leu Ile Gly Ala Cys Glu Phe Met Lys
 1           5           10          15
Asp Arg Leu Tyr Phe Ala Thr Leu Arg Asn Arg Pro Lys Ser Thr Val
 20          25          30
Asn Thr His Tyr Phe Ser Ile Asp Glu Glu Leu Val Tyr Glu Asn Phe
 35          40          45
Tyr Ala Asp Phe Gly Pro Leu Asn Leu Ala Met Val Tyr Arg Tyr Cys
 50          55          60
Cys Lys Leu Asn Lys Lys Leu Lys Ser Tyr Ser Leu Ser Arg Lys Lys
 65          70          75          80
Ile Val His Tyr Thr Cys Phe Asp Gln Arg Lys Arg Ala Asn Ala Ala
 85          90          95
Phe Leu Ile Gly Ala Tyr Ala Val Ile Tyr Leu Lys Lys Thr Pro Glu
100         105         110
Glu Ala Tyr Arg Ala Leu Leu Ser Gly Ser Asn Pro Pro Tyr Leu Pro
115         120         125

```

Phe Arg Asp Ala Ser Phe Gly Asn Cys Thr Tyr Asn Leu Thr Ile Leu
 130 135 140
 Asp Cys Leu Gln Gly Ile Arg Lys Gly Leu Gln His Gly Phe Phe Asp
 145 150 155 160
 Phe Glu Thr Phe Asp Val Asp Glu Tyr Glu His Tyr Glu Arg Val Glu
 165 170 175
 Asn Gly Asp Phe Asn Trp Ile Val Pro Gly Lys Phe Leu Ala Phe Ser
 180 185 190
 Gly Pro His Pro Lys Ser Lys Ile Glu Asn Gly Tyr Pro Leu His Ala
 195 200 205
 Pro Glu Ala Tyr Phe Pro Tyr Phe Lys Lys His Asn Val Thr Ala Val
 210 215 220
 Val Arg Leu Asn Lys Lys Ile Tyr Glu Ala Lys Arg Phe Thr Asp Ala
 225 230 235 240
 Gly Phe Glu His Tyr Asp Leu Phe Phe Ile Asp Gly Ser Thr Pro Ser
 245 250 255
 Asp Asn Ile Val Arg Arg Phe Leu Asn Ile Cys Glu Asn Thr Glu Gly
 260 265 270
 Ala Ile Ala Val His Cys Lys Ala Gly Leu Gly Arg Thr Gly Thr Leu
 275 280 285
 Ile Ala Cys Tyr Val Met Lys His Tyr Arg Phe Thr His Ala Glu Ile
 290 295 300
 Ile Ala Trp Ile Arg Ile Cys Arg Pro Gly Ser Ile Ile Gly Pro Gln
 305 310 315 320
 Gln His Phe Leu Glu Glu Lys Gln Ala Ser Leu Trp Val Gln Gly Asp
 325 330 335
 Ile Phe Arg Ser Lys Leu Lys Asn Arg Pro Ser Ser Glu Gly Ser Ile
 340 345 350
 Asn Lys Ile Leu Ser Gly Leu Asp Asp Met Ser Ile Gly Gly Asn Leu
 355 360 365
 Ser Lys Thr Gln Asn Met Glu Arg Phe Gly Glu Val Ser Phe Pro
 370 375 380

<210> 90

<211> 4624

<212> DNA

<213> Homo sapiens

<400> 90

cacggaacag ccctcctggg gtccccacga gccgcgtcct gctgtgcccc ggcgccctacg 60
 cagcagcggc cgcggccgcg gtgggcacgc acggttaccc cgggcagctc cggccgccag 120
 ctgcagcccc gtgcctcgg ccgcgccagc cggctgcggg cacctggggg cgggctgggg 180
 gcgcgggccc cggcaggagg cgctgtagcg agggtgcgg cgccggtcct gcggcggccg 240
 cgggaggcag cggggcaggc gctgtgggcc gggctcctcc tccggtcct gcgcgaccgc 300
 ctcccgccgg gctctgccgg cgcgcgcgt cccgcagcg ccgctctgcg cccgcgcgcc 360
 cgagcgcccc cgcggggctg gcgggagcct cggcgggcgc gcgggcgcgc ggggccatgg 420
 tcgtggcccc ctgacgggcc gcggcgcct ccatgaagcg gaaaagcgag cggcggtcga 480
 gctgggcccgc cgcgcctccc tgctcgcggc gctgctcgtc gacctcgccg ggtgtgaaga 540
 agatccgcag ctccacgcag caagaccgc gccgcggga cccccaggac gacgtgtacc 600
 tggacatcac cgatcgctt tgttttgcca ttctctacag cagaccaaag agtgcacaa 660
 atgtacatta ttacgcata gataatgaac ttgaatatga gaacttctac gcagattttg 720
 gaccactcaa tctggcaatg gtttacagat attgttgcaa gatcaataag aaattaaagt 780
 ccattacaat gtttaaggaag aaaattgttc attttactgg ctctgatcag agaaaacaag 840
 caaatgctgc cttccttggg ggtatgcata tgggtatata tttggggaga accccagaag 900
 aagcatatag aatattaatc tttggagaga catctatat tcttttcaga gatgctgcct 960
 atggaagtgg caatttctac attacacttc ttgactgttt tcatgcagta aagaaggcaa 1020
 tgcagtatgg cttccttaat ttcaactcat ttaaccttga tgaatatgaa cactatgaaa 1080

aagcagaaaa	tggagatttta	aattggataa	taccagaccg	atttattgcc	ttctgtggac	1140
ctcattcaag	agccagactt	gaaagtgggt	accaccaaca	ttctcctgag	acttatattc	1200
aatatatttaa	gaatcacaa	gttactacca	ttattcgtct	gaataaaaagg	atgtatgatg	1260
ccaaacgctt	tacggatgct	ggcttcgata	accatgatct	tttctttgcg	gatggcagca	1320
cccctactga	tgccattgtc	aaagaattcc	tagatatctg	tgaaaatgct	gagggtgcca	1380
ttgcagtaca	ttgcaaagct	ggccttgggt	gcacgggcac	tctgatagcc	tgctacatca	1440
tgaagcatta	caggatgaca	gcagccgaga	ccattgctgt	ggtcaggatc	tgacagacctg	1500
gctcgggtgat	tgggcctcag	cagcagtttt	tgggtgatgaa	gcaaaccaac	ctctggctgg	1560
aaggggacta	ttttcgtcag	aagttaaagg	ggcaggagaa	tggacaacac	agagcagcct	1620
tctccaaact	tctctctggc	gttgatgaca	tttccataaa	tggggtcgag	aatcaagatc	1680
agcaagaacc	cgaaccgtac	agtgatgatg	acgaaatcaa	tggagtgaca	caaggtgata	1740
gacttcgggc	cttgaaaagc	agaagacaat	ccaaaacaaa	cgctattcct	ctcacagtaa	1800
ttcttcaatc	cagtgttcag	agctgtaaaa	catctgaacc	taacatttct	ggcagtgcag	1860
gcattactaa	aagaaccacc	agatctgctt	caaggaaaag	cagtgttaaa	agtctctcca	1920
tttcaaggac	taaaacagtc	ttgcgttaag	taaaaacctg	tgaccagagc	tgaaggaaga	1980
ctctaggact	gaaaactgca	acagaaatta	gcacaatttg	aaaacaaaac	aaaattgcaa	2040
aagccttagt	tgctttttcc	acctaagaag	ttgatcaatg	gagaaaatgt	ccactggagt	2100
ttgaataatg	aacttttagt	ttgggtgcaa	gcaaagtact	cagagaaggg	tccagctctc	2160
aagctgaatg	acaacatgct	tgttgtaa	ttagtctcag	gtgtaaatac	ccaagccctc	2220
tggtagccag	ggagctggct	ggtctgtggt	gcatgtgtgt	ccctgtgatg	gcaatcattg	2280
tagttgctgg	ccttcagaag	aattgaggat	ctgatggagt	ttttttatgt	atttattttc	2340
tgttcacctt	gtgacctgt	gtcaaaattt	ataaagatac	aaaaggcatt	actgaaattg	2400
tactttctgt	aatttgatac	tatttggctt	aatcatcttc	acttgactat	ttgtaatact	2460
gttgtaatgt	taactctgtt	aagtacccaa	gctgcttgtc	ttccaccaa	gagtgcctta	2520
ttacaagaa	tctgtgaaaa	tcacatttaa	acactgttgc	atgttgtaag	accaggtggt	2580
accttagtaa	cctaaaactt	gcaagagaat	attaatggta	gctttagaag	actcaggagg	2640
agaaactgac	ttcagagttg	gaagatgttg	caagtcgttc	ctttttctgt	ccttcaggga	2700
ctgaagaact	gggaggctgc	ccattgtttg	gttgccagtc	atacaaatta	aatcatatt	2760
tccttccatg	aatggaagaa	acacactatt	ggtttttccc	cttggaacaa	gcaatcccaa	2820
ataatgtcgg	cttacaaaaa	aaaaaagtta	ccactttttt	agagtccttc	cctgtaacat	2880
tggatttttt	ttttccctta	tgagatccac	ctaaggccat	tgacgtggcc	tgcatctca	2940
gtgacaatga	tctgcttctg	gatctcactg	ttgcctttgg	ttagggaaca	caactagtaa	3000
ctctgcagag	tgccttctcc	cgcagcccta	ctggaacaca	gcagagtctg	tgccatgaag	3060
cagttacaga	aacagaattg	atgtgctgcc	aaaaaaaaaa	aaaaaatggg	gcccgaata	3120
aaagaatata	tagtactcac	ctcagttcct	tccataagaa	gtgggtggtt	taatgattgt	3180
taagccattt	ttgcctgtgc	cgggagcatg	gagggctgag	atgtcgacag	gcagtgggaa	3240
acaaatgccc	tcctaagcca	caaggcgtgc	gccagattag	taggcaactc	cattttaaga	3300
agctgccttt	ttcacaaaac	tggagaagaa	aaaagcggtt	ggaataaaca	agttaaaagt	3360
ctttaatgca	aaaagtaatt	gaaaggcagt	gcctccattt	tgggtgactt	tcttgggaaga	3420
aagtataaaa	ttgaccggca	tcattgagaga	cgggaagatgc	cgtgttctca	gccaaacaag	3480
caactctttc	cccgccaggc	actgtcgggt	ggggtcaggc	cagcttttaa	acactgggga	3540
ctggatcaca	gaaaaacagt	ggttttctgt	ccctggaaat	gaataggcac	aaagaccac	3600
ttggctgtgg	gcagactact	cttcaataag	atttgggtgg	gaggagggaac	attccttttg	3660
ctattttgag	ctgagacaat	ataaatattc	aaactgtgcc	atgcataaag	cattgaattc	3720
tcagggcacc	tcttcttccc	cttaccctt	ttaaggccat	cccctccatt	aataataatc	3780
caggtagttg	tgaaaatcgt	gcttctatct	gatcccttct	tagtttggtt	tttcatccca	3840
tcagaacaag	taaacgtagg	cgccacagct	cttgtgagta	ctgtctccct	cacggtgaat	3900
gagcctcctg	gtgtttcgtc	caagaaaaga	aaggggtgtca	ctggaaccac	agcccttttt	3960
cattttataa	actgcctctt	catgttgctt	gctcaagttt	ccacctagaa	ttgctatcac	4020
tgtggctctt	tctaaaaatc	tttctattta	actggttcac	tgaaattagt	catagaaaac	4080
ttgtgatttg	gtgaagaggc	attccttgta	ataaccaa	gacttgggat	ggtgtgcata	4140
gcaagggcag	tgttacactt	atgaggactg	tctctagcat	ccaggaagtc	tctgggtctg	4200
agggatggaa	agttcttctt	gctatgaatg	agagtggact	cttccctcca	cccccaactg	4260
aaaccacaaa	caaccagaat	cttctggat	tctgacttag	agtcgttggt	atagaagacc	4320
ttgttgctat	ggaacatgaa	actgtgtgtc	agatggagag	atccccctaa	cctaagagcc	4380
ttaaatagcc	ctgaaagtac	actgggacgg	tttgcgatgg	aattaaaatt	ggaagtgaat	4440
atttttaggt	gctcttgaag	ctttctgggg	actcaaaatt	atcaaaagtc	agggacagtc	4500
cggaggaaga	gcgtctgcaa	aactgggttc	ctagaagtat	agacggactt	agctttttgt	4560

agaatttggg gaggagcagc gcctcgtgag agcagaatgg cctggcgtgg ccagtgccttc 4620
ccgg 4624

<210> 91

<211> 498

<212> PRT

<213> Homo sapiens

<400> 91

Met Lys Arg Lys Ser Glu Arg Arg Ser Ser Trp Ala Ala Ala Pro Pro
1 5 10 15
Cys Ser Arg Arg Cys Ser Ser Thr Ser Pro Gly Val Lys Lys Ile Arg
20 25 30
Ser Ser Thr Gln Gln Asp Pro Arg Arg Arg Asp Pro Gln Asp Asp Val
35 40 45
Tyr Leu Asp Ile Thr Asp Arg Leu Cys Phe Ala Ile Leu Tyr Ser Arg
50 55 60
Pro Lys Ser Ala Ser Asn Val His Tyr Phe Ser Ile Asp Asn Glu Leu
65 70 75 80
Glu Tyr Glu Asn Phe Tyr Ala Asp Phe Gly Pro Leu Asn Leu Ala Met
85 90 95
Val Tyr Arg Tyr Cys Cys Lys Ile Asn Lys Lys Leu Lys Ser Ile Thr
100 105 110
Met Leu Arg Lys Lys Ile Val His Phe Thr Gly Ser Asp Gln Arg Lys
115 120 125
Gln Ala Asn Ala Ala Phe Leu Val Gly Cys Tyr Met Val Ile Tyr Leu
130 135 140
Gly Arg Thr Pro Glu Glu Ala Tyr Arg Ile Leu Ile Phe Gly Glu Thr
145 150 155 160
Ser Tyr Ile Pro Phe Arg Asp Ala Ala Tyr Gly Ser Cys Asn Phe Tyr
165 170 175
Ile Thr Leu Leu Asp Cys Phe His Ala Val Lys Lys Ala Met Gln Tyr
180 185 190
Gly Phe Leu Asn Phe Asn Ser Phe Asn Leu Asp Glu Tyr Glu His Tyr
195 200 205
Glu Lys Ala Glu Asn Gly Asp Leu Asn Trp Ile Ile Pro Asp Arg Phe
210 215 220
Ile Ala Phe Cys Gly Pro His Ser Arg Ala Arg Leu Glu Ser Gly Tyr
225 230 235 240
His Gln His Ser Pro Glu Thr Tyr Ile Gln Tyr Phe Lys Asn His Asn
245 250 255
Val Thr Thr Ile Ile Arg Leu Asn Lys Arg Met Tyr Asp Ala Lys Arg
260 265 270
Phe Thr Asp Ala Gly Phe Asp His His Asp Leu Phe Phe Ala Asp Gly
275 280 285
Ser Thr Pro Thr Asp Ala Ile Val Lys Glu Phe Leu Asp Ile Cys Glu
290 295 300
Asn Ala Glu Gly Ala Ile Ala Val His Cys Lys Ala Gly Leu Gly Arg
305 310 315 320
Thr Gly Thr Leu Ile Ala Cys Tyr Ile Met Lys His Tyr Arg Met Thr
325 330 335
Ala Ala Glu Thr Ile Ala Trp Val Arg Ile Cys Arg Pro Gly Ser Val
340 345 350
Ile Gly Pro Gln Gln Gln Phe Leu Val Met Lys Gln Thr Asn Leu Trp
355 360 365
Leu Glu Gly Asp Tyr Phe Arg Gln Lys Leu Lys Gly Gln Glu Asn Gly
370 375 380
Gln His Arg Ala Ala Phe Ser Lys Leu Leu Ser Gly Val Asp Asp Ile

385		390		395		400
Ser Ile Asn Gly Val	Glu Asn Gln Asp	Gln Gln Glu Pro	Glu Pro Tyr			
	405		410		415	
Ser Asp Asp Asp Glu	Ile Asn Gly Val	Thr Gln Gly Asp	Arg Leu Arg			
	420	425	430			
Ala Leu Lys Ser Arg	Arg Gln Ser Lys	Thr Asn Ala Ile	Pro Leu Thr			
	435	440	445			
Val Ile Leu Gln Ser	Ser Val Gln Ser	Cys Lys Thr Ser	Glu Pro Asn			
	450	455	460			
Ile Ser Gly Ser Ala	Gly Ile Thr Lys	Arg Thr Thr Arg	Ser Ala Ser			
465	470	475	480			
Arg Lys Ser Ser Val	Lys Ser Leu Ser	Ile Ser Arg Thr	Lys Thr Val			
	485	490	495			
Leu Arg						

<210> 92

<211> 4960

<212> DNA

<213> Homo sapiens

<400> 92

```

cacggaacag cctcctctggg gtccccacga gccgcgtcct gctgtgcccc ggcgcctacg 60
cagcagcggc cgcggcccgcg gtgggcacgc acggttaccc cgggcagctc cggccgccag 120
ctgcagcccc gtgcctctcg ccgcgccagc cggctgcggg cacctggggg cgggctgggg 180
gcgccggccg cggcaggagg cgctgtagcg agggctgcgg cgccggctct gcgccggccg 240
cgggaggcag cggggcaggc gctgtgggccc gggctctctc tccggctcct gcgccagccg 300
ctcccgcggg gctctgcggg cgcccgcgct cccgcagcgg ccgctctgcg cccgcgcgcc 360
cgagcgcggc cgcggggctg gcgggagcct cgccggggcg gcgggcgcgc gggggccatg 420
tcgtggcccc ctgacggggc gcggccgcct ccatgaagcg gaaaagcgag cggcggtcga 480
gctggggcgc cgcgcccccc tgctcgcggc gctgctcgtc gacctcgccg ggtgtgaaga 540
agatccgcag ctccacgcag caagaccgc gccgcgggga ccccaggac gacgtgtacc 600
tggacatcac cgatcgccct tgttttgcca ttctctacag cagaccaaag agtgcacaa 660
atgtacatta ttccagcata gataatgaac ttgaatatga gaacttctac gcagattttg 720
gacctcaaa tctggcaatg gtttacagat attgttgcaa gatcaataag aaattaaagt 780
cattacaat gttaaggaag aaaattgttc attttactgg ctctgatcag agaaaacaag 840
caaatgctgc ctcccttggt ggatgtcaca tggttatata tttggggaga accccagaag 900
aagcatatag aatattaatc ttggagaga catctatat tcctttcaga gatgtgcct 960
atggaagtgt caatttctac attacacttc ttgactgttt tcatgcagta aagaaggcaa 1020
tgcagtatgg ctcccttaat ttcaactcat ttaaccttga tgaatatgaa cactatgaaa 1080
aagcagaaaa tggagattta aattggataa taccagaccg atttattgcc ttctgtggag 1140
ctcattcaag agccagactt gaaagtgggt accaccaaca ttctcctgag acttatattc 1200
aatattttta gaatcacaat gttactacca ttattcgtct gaataaaaag atgtatgatg 1260
ccaaacgctt tacggatgct ggcttcgac accatgatct tttcttttgc gatggcagca 1320
cccctactga tgccattgtc aaagaattcc tagatatctg tgaaaatgct gagggtgcca 1380
ttgcagtaca ttgcaaagct ggccttggtc gcacgggcac tctgatagcc tgctacatca 1440
tgaagcatta caggatgaca gcagccgaga ccattgcgtg ggtcaggatc tgcagacctg 1500
gctcgggtgat tgggcctcag cagcagtttt tgggtgatgaa gcaaaccaac ctctggctgg 1560
aaggggacta ttttcgtcag aagttaaagg ggcaggagaa tggacaacac agagcagcct 1620
tctccaaact tctctctggc gttgatgaca ttccataaa tggggctcgag aatcaagatc 1680
agcaagaacc cgaaccgtac agtgatgatg acgaaatcaa tggagtgaca caaggtgata 1740
gacttcgggc cttgaaaagc agaagacaat ccaaaaacaa cgctattcct ctcaccgatg 1800
gttggtgtgc ccaggctgtc acctttctag accggcttct gatctggctc gggatccaca 1860
aggactagac ctgcggggaa ggtctctctc ggacacgccc gttgcccact gcaagttctc 1920
tccaggtgca attgaagcct ctccagcggc gaggccgcca tgtggagaga gcaggcaggc 1980
ccactgctgc tgagaacagg gcaggcacgg cagctccttg ttctgccttt cccagcttcg 2040
gagacgcagg ctccagctgct ccgaagcacc tgccagcacc gcacagtaca gtttcagagg 2100

```

```

acagcagctct ccttcccggtg aagctcccat gtgctggaat ggcattggact tgctgatcaa 2160
cagaaggaaa tggctctgaag tctgaccagc acaagggaagg aggcctggctg gctcagaggg 2220
gcccaccttg cgtggaatga aaacgcaaaa ggctcatgag caacattagg ctagaggggt 2280
cttgttcaaa gcatccaact ctgacttcgg aggcattccc agccggcagc agtgtgtcca 2340
gcctgcctct tcccaggttg gtctgacatg cagcttaggc tttcatcca agttaggtac 2400
tgacccctcc ctcttgggca gcacctccct ttttaaaaaa attttttttt cttccaaaga 2460
cagagtcttg ctcttgttgt ccaggctgga gtgcagtggc gcgatctagg ctactgcaa 2520
cctccttctc ccagggtcaa gcgactctcc tgcctcagcc tcctgagtag ctgggattat 2580
aggcgtctgc caccacgccc ggctaatttc tgtattttta gtagagacag ggtttcacca 2640
tggtggccag gctggtctcg aactcctgac ctcaagtgat ctgcctgctt tggcctccca 2700
aagtgtctgg attacaggtg tcagccaccg caccagcca agcaccctta tctctagagg 2760
atctggcccc ccagcccagt tactgcaggg cagctttccc cactggtga caggctgtgc 2820
gcagcagccc caggacctca ccctgagctg agtcttcagg agccgccctg gtggcacaac 2880
tcagacaccc ctgaggccta gcagtcaact cctgattcag acatgatcca gtccagcctg 2940
ggcttggcta taaccagctc aaacttgctt gacctccact tttcaggaga cttggggacg 3000
acagccctca tcggcgtctt tcatgggggt aatctgcttg agtctaagtc gccagccaga 3060
aacgtggtgc ccagggtgcc ctgcctcagg acatgtccac acccagctca caagcacctg 3120
aggagtccgg ccggggcact gtggtccaaa aggtcctgcc gcctccgcat ctgactgtcc 3180
caacggcatg ctggtgacac cccctgccc ttcgcttctg tcctccctgg cttctctggg 3240
gcacttgggg ctatgtacaa cctggcacga tccagaaagg gtgcaaacia aatgcctaca 3300
tccaggcaca cgaccaagtc agcgagagct agccctggta agcaaacata gccattaca 3360
ggttcagaac gtgcaccggg tccccaaaa ctgtcttcaa ccacatgact caacagctct 3420
atgggatagg aactgtcagt gtttttgcaa ctgcaacatt aaaccaagtg ctgtgggctt 3480
ttcaagtatt attcacaaca ctaaaggaaa gtttcttcaa agggctctct ggctaattct 3540
caaagccgca gttaggcaaa atgacagtgt gacagcttca aagccactga ctcatgacac 3600
agccctgatg ttgtaccggc taggttcaga tttcagaaat cagggcactt gcatccattg 3660
ccttttccag gaaagggaag aaaacactca gttgataaac cttagtactc agataataaa 3720
taagagacca aaagtaggct atcacccaaa gcaaacatcc ttaactgacc ctaacgtgta 3780
tggattcaac tttgattatt caacaaaatc atgaccgact gctgtggcct ggagtaacca 3840
aaggactgtt ttctctacac aaagtcagga gcgaatacca acctttattt gcaactgggt 3900
tccagttcaa agccacctta gacagtgtgg caaagtggga aaaagcacag atcctgggac 3960
caaggttcag attccatctc aagcgagcat atgaactgtg tgacaacagg cagacagtac 4020
ctctgtgtct atgagaaaagc ggggagagca acaccccagc ttctagcagc tctacagctg 4080
cctggacctg caggccctcc tagggccact tcctccccag cacagtgtgt gttcccgggc 4140
gtgtgtggct ctgggtccag ctctgttcag ggtgggactc cagggtgaatt actgaacctc 4200
tgagggtgtac ccccaacccc aaactttcac caaaagcaat aaagaggaac tctagaactg 4260
gagccaggac taagttagaa aaactgctta taagtgctta ataaatacta gttatttaca 4320
acttttgcct aagccgaggg cagaggcctt tgtacgcagc tgccgaactc tgactctagt 4380
tctgcggaag aaaaggatgc ggtatttgc tttgccaatga tccctttcca tttgattggc 4440
aggttaaata acatggtttt tgaagtcaca tacttaatat tcttctaaa aaccacccaa 4500
acactagatg tgtgtgtgca cacacacaga aaccacgggg tagtttaaata caccattaaa 4560
aatcaacgct ttctctgatt ctgtgtcaca gagtgggtgc cagtggctac aattttttaa 4620
tgattgggta agtgaiaacc agaactcaaa atattccagg agagaagata acatttacaa 4680
gtaaacagta agtgcaattg tatttttaatt tcttgggtct cgaaaactca gctgtgactg 4740
ctttccatta acagttccag ctctatgtgt tctctctaac gctaaaggca cagccccgg 4800
gaatctactg ctctctaaga gtctccatgg agtctatttt acaacctcct ttccctccat 4860
gcttccgagg aggagtctat actatctcta tatacacatt ttaaacatta ttcttcattt 4920
gaaattcctt caataaaaac acagtcacca ttaaaaaaaa 4960

```

<210> 93

<211> 471

<212> PRT

<213> Homo sapiens

<400> 93

```

Met Lys Arg Lys Ser Glu Arg Arg Ser Ser Trp Ala Ala Ala Pro Pro
 1             5             10             15
Cys Ser Arg Arg Cys Ser Ser Thr Ser Pro Gly Val Lys Lys Ile Arg

```

			20					25				30			
Ser	Ser	Thr	Gln	Gln	Asp	Pro	Arg	Arg	Arg	Asp	Pro	Gln	Asp	Asp	Val
		35					40					45			
Tyr	Leu	Asp	Ile	Thr	Asp	Arg	Leu	Cys	Phe	Ala	Ile	Leu	Tyr	Ser	Arg
	50					55					60				
Pro	Lys	Ser	Ala	Ser	Asn	Val	His	Tyr	Phe	Ser	Ile	Asp	Asn	Glu	Leu
65					70					75					80
Glu	Tyr	Glu	Asn	Phe	Tyr	Ala	Asp	Phe	Gly	Pro	Leu	Asn	Leu	Ala	Met
				85					90						95
Val	Tyr	Arg	Tyr	Cys	Cys	Lys	Ile	Asn	Lys	Lys	Leu	Lys	Ser	Ile	Thr
			100					105					110		
Met	Leu	Arg	Lys	Lys	Ile	Val	His	Phe	Thr	Gly	Ser	Asp	Gln	Arg	Lys
		115					120					125			
Gln	Ala	Asn	Ala	Ala	Phe	Leu	Val	Gly	Cys	Tyr	Met	Val	Ile	Tyr	Leu
	130					135					140				
Gly	Arg	Thr	Pro	Glu	Glu	Ala	Tyr	Arg	Ile	Leu	Ile	Phe	Gly	Glu	Thr
145					150					155					160
Ser	Tyr	Ile	Pro	Phe	Arg	Asp	Ala	Ala	Tyr	Gly	Ser	Cys	Asn	Phe	Tyr
				165					170					175	
Ile	Thr	Leu	Leu	Asp	Cys	Phe	His	Ala	Val	Lys	Lys	Ala	Met	Gln	Tyr
			180					185					190		
Gly	Phe	Leu	Asn	Phe	Asn	Ser	Phe	Asn	Leu	Asp	Glu	Tyr	Glu	His	Tyr
		195					200					205			
Glu	Lys	Ala	Glu	Asn	Gly	Asp	Leu	Asn	Trp	Ile	Ile	Pro	Asp	Arg	Phe
	210					215					220				
Ile	Ala	Phe	Cys	Gly	Pro	His	Ser	Arg	Ala	Arg	Leu	Glu	Ser	Gly	Tyr
225					230					235					240
His	Gln	His	Ser	Pro	Glu	Thr	Tyr	Ile	Gln	Tyr	Phe	Lys	Asn	His	Asn
				245					250					255	
Val	Thr	Thr	Ile	Ile	Arg	Leu	Asn	Lys	Arg	Met	Tyr	Asp	Ala	Lys	Arg
			260					265					270		
Phe	Thr	Asp	Ala	Gly	Phe	Asp	His	His	Asp	Leu	Phe	Phe	Ala	Asp	Gly
		275					280					285			
Ser	Thr	Pro	Thr	Asp	Ala	Ile	Val	Lys	Glu	Phe	Leu	Asp	Ile	Cys	Glu
		290				295					300				
Asn	Ala	Glu	Gly	Ala	Ile	Ala	Val	His	Cys	Lys	Ala	Gly	Leu	Gly	Arg
305					310					315					320
Thr	Gly	Thr	Leu	Ile	Ala	Cys	Tyr	Ile	Met	Lys	His	Tyr	Arg	Met	Thr
				325					330					335	
Ala	Ala	Glu	Thr	Ile	Ala	Trp	Val	Arg	Ile	Cys	Arg	Pro	Gly	Ser	Val
			340					345					350		
Ile	Gly	Pro	Gln	Gln	Gln	Phe	Leu	Val	Met	Lys	Gln	Thr	Asn	Leu	Trp
		355					360					365			
Leu	Glu	Gly	Asp	Tyr	Phe	Arg	Gln	Lys	Leu	Lys	Gly	Gln	Glu	Asn	Gly
		370				375									

<210> 94
 <211> 834
 <212> DNA
 <213> Homo sapiens

<400> 94

```

cttttcctgt atttttttgc ttcattcttg gtgtttcgct gactgctgac cactgaccca 60
ccgccttgat gacagcaccc tcgtgtgcct tcccagttca gttccggcag ccctcagtca 120
gcggcctctc gcagataacc aaaagcctgt atatcagcaa tgggtgtggcc gccacaaca 180
agctcatgct gtctagcaac cagatcacca tggatcatcaa tgtctcagtg gaggtagtga 240
acaccttgta tgaggatata cagtacatgc aggtacctgt ggctgactcc cctaactcac 300
gtctctgtga cttctttgac cctattgctg accatatcca cagcgtggag atgaagcagg 360
gccgtacttt gctgcactgt gctgctgggt tgagccgctc agctgccctg tgcctcgcct 420
acctcatgaa gtaccacgcc atgtccctgc tggacgccc cactgggacc aagtcatgcc 480
ggcccatcat ccgacccaac agcggctttt gggagcagct catccactat gagttccaat 540
tgtttggaac gaacactgtg cacatgggtc gttccccagt gggaatgatc cctgacatct 600
atgagaagga agtccgtttg atgattccac tgtgagccat cccacgagcc cctgcattgg 660
agtcagaggt acagatctat tgttgatctt acaccaagat ccaaacttga acattctact 720
tttgattgata cagaaaaaaaa cagatgatgc cttttatgag cacaaaaaag agttgctgta 780
gcttttaact ttataatcca ttttttttca gattaaacta attgtgagat ggtg      834
  
```

<210> 95
 <211> 188
 <212> PRT
 <213> Homo sapiens

<400> 95

```

Met Thr Ala Pro Ser Cys Ala Phe Pro Val Gln Phe Arg Gln Pro Ser
1      5      10      15
Val Ser Gly Leu Ser Gln Ile Thr Lys Ser Leu Tyr Ile Ser Asn Gly
20     25     30
Val Ala Ala Asn Asn Lys Leu Met Leu Ser Ser Asn Gln Ile Thr Met
35     40     45
Val Ile Asn Val Ser Val Glu Val Val Asn Thr Leu Tyr Glu Asp Ile
50     55     60
Gln Tyr Met Gln Val Pro Val Ala Asp Ser Pro Asn Ser Arg Leu Cys
65     70     75     80
Asp Phe Phe Asp Pro Ile Ala Asp His Ile His Ser Val Glu Met Lys
85     90     95
Gln Gly Arg Thr Leu Leu His Cys Ala Ala Gly Val Ser Arg Ser Ala
100    105    110
Ala Leu Cys Leu Ala Tyr Leu Met Lys Tyr His Ala Met Ser Leu Leu
115    120    125
Asp Ala His Thr Trp Thr Lys Ser Cys Arg Pro Ile Ile Arg Pro Asn
130    135    140
Ser Gly Phe Trp Glu Gln Leu Ile His Tyr Glu Phe Gln Leu Phe Gly
145    150    155    160
Lys Asn Thr Val His Met Val Ser Ser Pro Val Gly Met Ile Pro Asp
165    170    175
Ile Tyr Glu Lys Glu Val Arg Leu Met Ile Pro Leu
180    185
  
```

<210> 96
 <211> 926
 <212> DNA
 <213> Homo sapiens

<400> 96

```

ccccgcgct cctcctccct gtaacatgcc atagtgcgcc tgcgaccaca cggccggggc 60
gctagcggtc gccttcagcc accatgggga atgggatgaa caagatcctg cccggcctgt 120
acatcggcaa cttcaaagat gccagagacg cggaacaatt gagcaagaac aaggtgacac 180
atattctgtc tgtccacgat agtgccaggc ctatgttgga gggagttaaa tacctgtgca 240
tcccagcagc ggattcacca tctcaaaacc tgacaagaca tttcaaagaa agtattaaat 300
tcattcacga gtgccggctc cgcggtgaga gctgccttgt aactgcctg gccgggggtct 360
ccaggagcgt gacactgggtg atcgcataca tcatgaccgt cactgacttt ggctgggagg 420
atgccctgca caccgtgctg gctgggagat cctgtgccaa cccaacgtg ggcttccaga 480
gacagctcca ggagtttgag aagcatgagg tccatcagta tcggcagtggt ctgaagggaag 540
aatatggaga gagccctttg caggatgcag aagaagccaa aaacattctg gccgctccag 600
gaattctgaa gttctgggccc tttctcagaa gactgtaatg tacctgaagt ttctgaaata 660
ttgcaaaccg gcagagttta ggctgggtgct gccaaaaaga aaagcaacat agagtttaag 720
tatccagtag tgatttgtaa acttggtttt catttgaagc tgaatatata cgtagtcatg 780
tttatgttga gaactaagga tattcttttag caagagaaaa tattttcccc ttatccccac 840
tgctgtggag gtttctgtac ctgcgttgga tgctgtgaag gatcccgga gccttgccgc 900
actgccttgt ggggtgcttg gcgctc

```

926

<210> 97

<211> 184

<212> PRT

<213> Homo sapiens

<400> 97

```

Met Gly Asn Gly Met Asn Lys Ile Leu Pro Gly Leu Tyr Ile Gly Asn
1          5          10          15
Phe Lys Asp Ala Arg Asp Ala Glu Gln Leu Ser Lys Asn Lys Val Thr
20          25          30
His Ile Leu Ser Val His Asp Ser Ala Arg Pro Met Leu Glu Gly Val
35          40          45
Lys Tyr Leu Cys Ile Pro Ala Ala Asp Ser Pro Ser Gln Asn Leu Thr
50          55          60
Arg His Phe Lys Glu Ser Ile Lys Phe Ile His Glu Cys Arg Leu Arg
65          70          75          80
Gly Glu Ser Cys Leu Val His Cys Leu Ala Gly Val Ser Arg Ser Val
85          90          95
Thr Leu Val Ile Ala Tyr Ile Met Thr Val Thr Asp Phe Gly Trp Glu
100         105         110
Asp Ala Leu His Thr Val Arg Ala Gly Arg Ser Cys Ala Asn Pro Asn
115         120         125
Val Gly Phe Gln Arg Gln Leu Gln Glu Phe Glu Lys His Glu Val His
130         135         140
Gln Tyr Arg Gln Trp Leu Lys Glu Glu Tyr Gly Glu Ser Pro Leu Gln
145         150         155         160
Asp Ala Glu Glu Ala Lys Asn Ile Leu Ala Ala Pro Gly Ile Leu Lys
165         170         175
Phe Trp Ala Phe Leu Arg Arg Leu
180

```

<210> 98

<211> 4882

<212> DNA

<213> Homo sapiens

<400> 98

```

agaggaggaa attgttcttc gtctgataag acaacagtgg agaaaggacg catgctgttt 60

```

cttagggaca	cggttgactt	ccagatatga	ccatgtat	gtggcttaaa	ctcttggcat	120
ttggctttgc	ctttctggac	acagaagtat	ttgtgacagg	gcaaagccca	acaccttccc	180
ccactggatt	gactacagca	aagatgcccc	gtgttccact	ttcaagtga	cccttaccta	240
ctcacaccac	tgcatttctca	cccgaagca	cctttgaaag	agaaaatgac	ttctcagaga	300
ccacaacttc	tcttagtcca	gacaatactt	ccacccaagt	atccccggac	tctttggata	360
atgctagtgc	ttttaatacc	acaggtgttt	catcagtaca	gacgcctcac	cttcccacgc	420
acgcagactc	gcagacgccc	tctgctggaa	ctgacacgca	gacattcagc	ggctccgccc	480
ccaatgcaaa	actcaaccct	accccaggca	gcaatgctat	ctcagatgcc	taccttaatg	540
cctctgaaac	aaccactctg	agcccttctg	gaagcgctgt	catttcaacc	acaacaatag	600
ctactactcc	atctaagcca	acatgtgatg	aaaaatatgc	aaacatcact	gtggattact	660
tatataacaa	ggaaactaaa	ttattttacag	caaagctaaa	tgtaaatgag	aatgtggaat	720
gtggaaacaa	tacttgacaca	aacaatgagg	tgcataacct	tacagaatgt	aaaaatgcgt	780
ctgtttccat	atctcataat	tcatgtactg	ctcctgataa	gacattaata	ttagatgtgc	840
caccaggggt	tgaaaagttt	cagttacatg	attgtacaca	agttgaaaaa	gcagatacta	900
ctattttgtt	aaaatggaaa	aatattgaaa	cctttacttg	tgatacacag	aatattacct	960
acagattttca	gtgtggtaat	atgataattg	ataataaaga	aattaaatta	gaaaaccttg	1020
aacccgaaca	tgagtataag	tgtgactcag	aaatactcta	taataaccac	aagtttacta	1080
acgcaagtta	aattattttaa	acagattttg	ggagctccag	agagcctcag	attatttttt	1140
gtagaagtga	agctgcacat	caaggagtaa	ttacctggaa	tccccctcaa	agatcatttc	1200
ataattttac	ctctgtttat	ataaaagaga	cagaaaaaga	ttgcctcaat	ctggataaaa	1260
acctgatcaa	atatgatttg	caaaatttaa	aaccttatac	gaaatatgtt	ttatcattac	1320
atgcctacat	cattgcaaaa	gtgcaacgta	atggaagtgc	tgcaatgtgt	catttcacaa	1380
ctaaaagtgc	tcctccaagc	caggtctgga	acatgactgt	ctccatgaca	tcagataata	1440
gtatgcatgt	caagtgtagg	cctcccagg	accgtaatgg	cccccatgaa	cgttaccatt	1500
tggaagtga	agctggaaat	actctgggta	gaaatgagtc	gcataagaat	tgcgatttcc	1560
gtgtaaaaga	tcttcaatat	tcaacagact	acacttttaa	ggcctatttt	cacaatggag	1620
actatcctgg	agaacccttt	atttttacatc	attcaacatc	ttataattct	aaggcactga	1680
tagcattttct	ggcattttctg	attatttgtga	catcaatagc	cctgcttggt	gttctctaca	1740
aaatctatga	tctacataag	aaaagatcct	gcaattttaga	tgaacagcag	gagcttggtg	1800
aaagggatga	tgaaaaacaa	ctgatgaatg	tggagccaat	ccatgcagat	attttggttg	1860
aaacttataa	gaggaagatt	gctgatgaag	gaagactttt	tctggctgaa	tttcagagca	1920
tcccgcggt	gttcagcaag	tttctataa	aggaagctcg	aaagcccttt	aaccagaata	1980
aaaaccgtta	tgttgacatt	cttcttatg	attataaccg	tgttgaactc	tctgagataa	2040
acggagatgc	aggttcaaac	tacataaatg	ccagctatat	tgatggtttc	aaagaacca	2100
ggaaatacat	tgctgcacaa	ggtcccagg	atgaaactgt	tgatgatttc	tggaggatga	2160
tttgggaaca	gaaagccaca	gttattgtca	tggtcactcg	atgtgaagaa	ggaaacagga	2220
acaagtgtgc	agaattctgg	ccgtcaatgg	aagagggcac	tcgggctttt	ggagatgttg	2280
ttgtaagat	caaccagcac	aaaagatgtc	cagattacat	cattcagaaa	ttgaacattg	2340
taaataaaaa	agaaaaagca	actggaagag	aggtgactca	cattcagttc	accagctggc	2400
cagaccacgg	ggtgcctgag	gacccctact	tgctcctcaa	actgagaagg	agagtgaatg	2460
ccttcagcaa	tttcttcagt	ggtcccatg	tggtgcactg	cagtgcctgg	gttgggcgca	2520
caggaacct	tatcggaatt	gatgccatgc	tagaaggcct	ggaagccgag	aacaaagtgg	2580
atgttttatg	ttatgttgtc	aagctaaggc	gacagagatg	cctgatgggt	caagtagagg	2640
cccagtacat	cttgatccat	caggcttttg	tggaaatacaa	tcagtttgga	gaaacagaag	2700
tgaatttgtc	tgaattacat	ccatatctac	ataacatgaa	gaaaagggat	ccaccagtg	2760
agccgtctcc	actagaggct	gaattccaga	gacttccctc	atataggagc	tggaggacac	2820
agcacattgg	aatcaagaa	gaaaataaaa	gtaaaaacag	gaattcta	gtcatcccat	2880
atgactataa	cagagtgcc	cttaaacatg	agctggaaat	gagtaaagag	agtgagcatg	2940
attcagatga	atcctctgat	gatgacagtg	attcagagga	accaagcaaa	tacatcaatg	3000
catcttttat	aatgagctac	tggaaacctg	aagtgatgat	tgctgctcag	ggaccactga	3060
aggagacct	tggtgacttt	tggcagatga	tcttccaaag	aaaagtcaaa	gttattgtta	3120
tgctgacaga	actgaaacat	ggagaccagg	aaatctgtgc	tcagtactgg	ggagaaggaa	3180
agcaaacata	tggagatatt	gaagttgacc	tgaaagacac	agacaaatct	tcaacttata	3240
cccttcgtgt	ctttgaactg	agacattcca	agaggaagaa	ctctcgaact	gtgtaccagt	3300
accaatatac	aaactggagt	gtggagcagc	ttcctgcaga	acccaaggaa	ttaatctcta	3360
tgattcaggt	cgtcaaacaa	aaacttcccc	agaagaattc	ctctgaagg	aacaagcatc	3420
acaagagtac	acctctactc	attcactgca	gggatggatc	tcagcaaacg	ggaatatttt	3480
gtgctttgtt	aaatctctta	gaaagtgcgg	aaacagaaga	ggtagtggat	atttttcaag	3540

```

tggtaaaagc tctacgcaaa gctaggccag gcatgggttc cacattcgag caatatcaat 3600
tcctatatga cgtcattgcc agcacctacc ctgctcagaa tggacaagta aagaaaaaca 3660
accatcaaga agataaaatt gaatttgata atgaagtgga caaagtaaag caggatgcta 3720
attgtgttaa tccacttggt gccccagaaa agctccctga agcaaaggaa caggctgaag 3780
gttctgaacc cagcagtggc actgaggggc cagaacattc tgtcaatggc cctgcaagtc 3840
cagctttaaa tcaagggttc taggaaaaga cataaatgag gaaactccaa acctcctgtt 3900
agctgttatt tctatTTTTg tagaagtagg aagtgaaaat aggtatacag tggattaatt 3960
aaatgcagcg aaccaatatt tgtagaaggg ttatatTTTA ctactgtgga aaaatatTTA 4020
agatagTTTT gccagaacag tttgtacaga cgtatgctta ttttaaaatt ttatctctta 4080
ttcagtaaaa aacaacttct ttgtaatcgt tatgtgtgta tatgtatgtg tgtatgggtg 4140
tgtgtttgtg tgagagacag agaaagagag agaattcttt caagtgaatc taaaagcttt 4200
tgcttttctt ttgtttttat gaagaaaaaa tacattttat attagaagtg ttaacttagc 4260
ttgaaggatc tgttttttaa aatcataaac tgtgtgcaga ctcaataaaa tcatgtacat 4320
ttctgaaatg acctcaagat gtctctcttg ttctactcat atatatctat cttatatact 4380
tactatTTTA cttctagaga tagtacataa aggtgggtat tgtgtgtatg ctactacaaa 4440
aaagttgtta actaaattaa cattgggaaa tcttatattc catatattag catttagtcc 4500
aatgtctttt taagcttatt taattaaaaa atttccagtg agcttatcat gctgtcttta 4560
catgggggtt tcaattttgc atgctcgatt attccctgta caatatttaa aatttattgc 4620
ttgatacttt tgacaacaaa ttaggttttg tacaattgaa cttaaataaa tgtcattaaa 4680
ataaataaat gcaatatgta ttaatatTTA ttgtataaaa atagaagaat acaaacatat 4740
ttgttaaata ttacatatg aaattttaata tagctatttt tatggaattt ttcatgata 4800
tgaaaaatat gatattgcat atgcatagtt cccatgttaa atccattca taactttcat 4860
taaagcattt actttgaatt tc 4882

```

<210> 99

<211> 1256

<212> PRT

<213> Homo sapiens

<400> 99

```

Met Tyr Leu Trp Leu Lys Leu Leu Ala Phe Gly Phe Ala Phe Leu Asp
 1           5           10           15
Thr Glu Val Phe Val Thr Gly Gln Ser Pro Thr Pro Ser Pro Thr Gly
 20           25           30
Leu Thr Thr Ala Lys Met Pro Ser Val Pro Leu Ser Ser Asp Pro Leu
 35           40           45
Pro Thr His Thr Thr Ala Phe Ser Pro Ala Ser Thr Phe Glu Arg Glu
 50           55           60
Asn Asp Phe Ser Glu Thr Thr Thr Ser Leu Ser Pro Asp Asn Thr Ser
 65           70           75           80
Thr Gln Val Ser Pro Asp Ser Leu Asp Asn Ala Ser Ala Phe Asn Thr
 85           90           95
Thr Gly Val Ser Ser Val Gln Thr Pro His Leu Pro Thr His Ala Asp
100           105           110
Ser Gln Thr Pro Ser Ala Gly Thr Asp Thr Gln Thr Phe Ser Gly Ser
115           120           125
Ala Ala Asn Ala Lys Leu Asn Pro Thr Pro Gly Ser Asn Ala Ile Ser
130           135           140
Asp Ala Tyr Leu Asn Ala Ser Glu Thr Thr Thr Leu Ser Pro Ser Gly
145           150           155           160
Ser Ala Val Ile Ser Thr Thr Thr Ile Ala Thr Thr Pro Ser Lys Pro
165           170           175
Thr Cys Asp Glu Lys Tyr Ala Asn Ile Thr Val Asp Tyr Leu Tyr Asn
180           185           190
Lys Glu Thr Lys Leu Phe Thr Ala Lys Leu Asn Val Asn Glu Asn Val
195           200           205
Glu Cys Gly Asn Asn Thr Cys Thr Asn Asn Glu Val His Asn Leu Thr
210           215           220

```

Glu Cys Lys Asn Ala Ser Val Ser Ile Ser His Asn Ser Cys Thr Ala
 225 230 235 240
 Pro Asp Lys Thr Leu Ile Leu Asp Val Pro Pro Gly Val Glu Lys Phe
 245 250 255
 Gln Leu His Asp Cys Thr Gln Val Glu Lys Ala Asp Thr Thr Ile Cys
 260 265 270
 Leu Lys Trp Lys Asn Ile Glu Thr Phe Thr Cys Asp Thr Gln Asn Ile
 275 280 285
 Thr Tyr Arg Phe Gln Cys Gly Asn Met Ile Phe Asp Asn Lys Glu Ile
 290 295 300
 Lys Leu Glu Asn Leu Glu Pro Glu His Glu Tyr Lys Cys Asp Ser Glu
 305 310 315 320
 Ile Leu Tyr Asn Asn His Lys Phe Thr Asn Ala Ser Lys Ile Ile Lys
 325 330 335
 Thr Asp Phe Gly Ser Pro Gly Glu Pro Gln Ile Ile Phe Cys Arg Ser
 340 345 350
 Glu Ala Ala His Gln Gly Val Ile Thr Trp Asn Pro Pro Gln Arg Ser
 355 360 365
 Phe His Asn Phe Thr Leu Cys Tyr Ile Lys Glu Thr Glu Lys Asp Cys
 370 375 380
 Leu Asn Leu Asp Lys Asn Leu Ile Lys Tyr Asp Leu Gln Asn Leu Lys
 385 390 395 400
 Pro Tyr Thr Lys Tyr Val Leu Ser Leu His Ala Tyr Ile Ile Ala Lys
 405 410 415
 Val Gln Arg Asn Gly Ser Ala Ala Met Cys His Phe Thr Thr Lys Ser
 420 425 430
 Ala Pro Pro Ser Gln Val Trp Asn Met Thr Val Ser Met Thr Ser Asp
 435 440 445
 Asn Ser Met His Val Lys Cys Arg Pro Pro Arg Asp Arg Asn Gly Pro
 450 455 460
 His Glu Arg Tyr His Leu Glu Val Glu Ala Gly Asn Thr Leu Val Arg
 465 470 475 480
 Asn Glu Ser His Lys Asn Cys Asp Phe Arg Val Lys Asp Leu Gln Tyr
 485 490 495
 Ser Thr Asp Tyr Thr Phe Lys Ala Tyr Phe His Asn Gly Asp Tyr Pro
 500 505 510
 Gly Glu Pro Phe Ile Leu His His Ser Thr Ser Tyr Asn Ser Lys Ala
 515 520 525
 Leu Ile Ala Phe Leu Ala Phe Leu Ile Ile Val Thr Ser Ile Ala Leu
 530 535 540
 Leu Val Val Leu Tyr Lys Ile Tyr Asp Leu His Lys Lys Arg Ser Cys
 545 550 555 560
 Asn Leu Asp Glu Gln Gln Glu Leu Val Glu Arg Asp Asp Glu Lys Gln
 565 570 575
 Leu Met Asn Val Glu Pro Ile His Ala Asp Ile Leu Leu Glu Thr Tyr
 580 585 590
 Lys Arg Lys Ile Ala Asp Glu Gly Arg Leu Phe Leu Ala Glu Phe Gln
 595 600 605
 Ser Ile Pro Arg Val Phe Ser Lys Phe Pro Ile Lys Glu Ala Arg Lys
 610 615 620
 Pro Phe Asn Gln Asn Lys Asn Arg Tyr Val Asp Ile Leu Pro Tyr Asp
 625 630 635 640
 Tyr Asn Arg Val Glu Leu Ser Glu Ile Asn Gly Asp Ala Gly Ser Asn
 645 650 655
 Tyr Ile Asn Ala Ser Tyr Ile Asp Gly Phe Lys Glu Pro Arg Lys Tyr
 660 665 670
 Ile Ala Ala Gln Gly Pro Arg Asp Glu Thr Val Asp Asp Phe Trp Arg
 675 680 685

Met Ile Trp Glu Gln Lys Ala Thr Val Ile Val Met Val Thr Arg Cys
 690 695 700
 Glu Glu Gly Asn Arg Asn Lys Cys Ala Glu Tyr Trp Pro Ser Met Glu
 705 710 715 720
 Glu Gly Thr Arg Ala Phe Gly Asp Val Val Val Lys Ile Asn Gln His
 725 730 735
 Lys Arg Cys Pro Asp Tyr Ile Ile Gln Lys Leu Asn Ile Val Asn Lys
 740 745 750
 Lys Glu Lys Ala Thr Gly Arg Glu Val Thr His Ile Gln Phe Thr Ser
 755 760 765
 Trp Pro Asp His Gly Val Pro Glu Asp Pro His Leu Leu Leu Lys Leu
 770 775 780
 Arg Arg Arg Val Asn Ala Phe Ser Asn Phe Phe Ser Gly Pro Ile Val
 785 790 795 800
 Val His Cys Ser Ala Gly Val Gly Arg Thr Gly Thr Tyr Ile Gly Ile
 805 810 815
 Asp Ala Met Leu Glu Gly Leu Glu Ala Glu Asn Lys Val Asp Val Tyr
 820 825 830
 Gly Tyr Val Val Lys Leu Arg Arg Gln Arg Cys Leu Met Val Gln Val
 835 840 845
 Glu Ala Gln Tyr Ile Leu Ile His Gln Ala Leu Val Glu Tyr Asn Gln
 850 855 860
 Phe Gly Glu Thr Glu Val Asn Leu Ser Glu Leu His Pro Tyr Leu His
 865 870 875 880
 Asn Met Lys Lys Arg Asp Pro Pro Ser Glu Pro Ser Pro Leu Glu Ala
 885 890 895
 Glu Phe Gln Arg Leu Pro Ser Tyr Arg Ser Trp Arg Thr Gln His Ile
 900 905 910
 Gly Asn Gln Glu Glu Asn Lys Ser Lys Asn Arg Asn Ser Asn Val Ile
 915 920 925
 Pro Tyr Asp Tyr Asn Arg Val Pro Leu Lys His Glu Leu Glu Met Ser
 930 935 940
 Lys Glu Ser Glu His Asp Ser Asp Glu Ser Ser Asp Asp Asp Ser Asp
 945 950 955 960
 Ser Glu Glu Pro Ser Lys Tyr Ile Asn Ala Ser Phe Ile Met Ser Tyr
 965 970 975
 Trp Lys Pro Glu Val Met Ile Ala Ala Gln Gly Pro Leu Lys Glu Thr
 980 985 990
 Ile Gly Asp Phe Trp Gln Met Ile Phe Gln Arg Lys Val Lys Val Ile
 995 1000 1005
 Val Met Leu Thr Glu Leu Lys His Gly Asp Gln Glu Ile Cys Ala Gln
 1010 1015 1020
 Tyr Trp Gly Glu Gly Lys Gln Thr Tyr Gly Asp Ile Glu Val Asp Leu
 1025 1030 1035 1040
 Lys Asp Thr Asp Lys Ser Ser Thr Tyr Thr Leu Arg Val Phe Glu Leu
 1045 1050 1055
 Arg His Ser Lys Arg Lys Asp Ser Arg Thr Val Tyr Gln Tyr Gln Tyr
 1060 1065 1070
 Thr Asn Trp Ser Val Glu Gln Leu Pro Ala Glu Pro Lys Glu Leu Ile
 1075 1080 1085
 Ser Met Ile Gln Val Val Lys Gln Lys Leu Pro Gln Lys Asn Ser Ser
 1090 1095 1100
 Glu Gly Asn Lys His His Lys Ser Thr Pro Leu Leu Ile His Cys Arg
 1105 1110 1115 1120
 Asp Gly Ser Gln Gln Thr Gly Ile Phe Cys Ala Leu Leu Asn Leu Leu
 1125 1130 1135
 Glu Ser Ala Glu Thr Glu Glu Val Val Asp Ile Phe Gln Val Val Lys
 1140 1145 1150

Ala Leu Arg Lys Ala Arg Pro Gly Met Val Ser Thr Phe Glu Gln Tyr
 1155 1160 1165
 Gln Phe Leu Tyr Asp Val Ile Ala Ser Thr Tyr Pro Ala Gln Asn Gly
 1170 1175 1180
 Gln Val Lys Lys Asn Asn His Gln Glu Asp Lys Ile Glu Phe Asp Asn
 1185 1190 1195 1200
 Glu Val Asp Lys Val Lys Gln Asp Ala Asn Cys Val Asn Pro Leu Gly
 1205 1210 1215
 Ala Pro Glu Lys Leu Pro Glu Ala Lys Glu Gln Ala Glu Gly Ser Glu
 1220 1225 1230
 Pro Thr Ser Gly Thr Glu Gly Pro Glu His Ser Val Asn Gly Pro Ala
 1235 1240 1245
 Ser Pro Ala Leu Asn Gln Gly Ser
 1250 1255

<210> 100

<211> 4543

<212> DNA

<213> Homo sapiens

<400> 100

```

agaggaggaa attgttcctc gtctgataag acaacagtgg agaaaggacg catgctgttt 60
cttagggaca cggctgactt ccagatatga ccatgtattt gtggcttaaa ctcttggcat 120
ttggctttgc ctttctggac acagaagtat ttgtgacagg gcaaagccca acaccttccc 180
ccactgatgc ctaccttaat gcctctgaaa caaccactct gagcccttct ggaagcgctg 240
tcatttcaac cacaacaata gctactactc catctaagcc aacatgtgat gaaaaatatg 300
caaacatcac tgtggattac ttatataaca aggaaactaa attatttaca gcaaagctaa 360
atgttaaatga gaatgtggaa tgtggaaaca atacttgcac aaacaatgag gtgcataacc 420
ttacagaatg taaaaatgcy tctgtttcca tatctcataa ttcatgtact gtccttgata 480
agacattaat attagatgtg ccaccagggg ttgaaaagtt tcagttacat gattgtacac 540
aagttgaaaa agcagatact actatttgtt taaaatggaa aaatattgaa acctttactt 600
gtgatacaca gaattattacc tacagatttc agtgtggtaa tatgatattt gataataaag 660
aaattaaatt agaaaacctt gaacccgaac atgagtataa gtgtgactca gaaatactct 720
ataataacca caagtttact aacgcaagta aaattattaa aacagatttt gggagtcagg 780
gagagcctca gattattttt tgtagaagtg aagctgcaca tcaaggagta attacctgga 840
atccccctca aagatcatctt cataatttta cctctgttta tataaaagag acagaaaaag 900
attgcctcaa tctggataaa aacctgatca aatatgattt gcaaaattta aaaccttata 960
cgaaatatgt tttatcatta catgcctaca tcattgcaaa agtgcaacgt aatggaagtg 1020
ctgcaatgtg tcatttcaca actaaaagtg ctctctcaag ccaggtctgg aacatgactg 1080
tctccatgac atcagataat agtatgcatg tcaagtgtag gcctcccagg gaccgtaatg 1140
gcccccatga acgttaccat ttggaagttg aagctggaaa tactctgggt agaaatgagt 1200
cgcataagaa ttgcgatttc cgtgtaaaag atcttcaata ttcaacagac tacactttta 1260
aggcctatth tcacaatgga gactatcctg gagaaccctt tattttacat cattcaacat 1320
cttataatth taaggcactg atagcatttc tggcatttct gattattgtg acatcaatag 1380
ccctgcttgt tgttctctac aaaatctatg atctacataa gaaaagatcc tgcaatttag 1440
atgaacagca ggagcttgtt gaaagggatg atgaaaaaca actgatgaat gtggagccaa 1500
tccatgcaga tattttgttg gaaacttata agagggaagt tgctgatgaa ggaagacttt 1560
ttctggctga atttcagagc atccccgctg tgttcagcaa gtttcctata aaggaagctc 1620
gaaagccctt taaccagaat aaaaaccgtt atgttgacat tcttccttat gattataacc 1680
gtgttgaaat ctctgagata aacggagatg caggggtcaaa ctacataaat gccagctata 1740
ttgatggtht caaagaaccc aggaataaca ttgctgcaca aggtcccagg gatgaaactg 1800
ttgatgattt ctggaggatg atttgggaac agaaagccac agttattgtc atgggtcactc 1860
gatgtgaaga aggaacacag aacaagtgtg cagaatactg gccgtcaatg gaagagggca 1920
ctcgggctth tggagatgtt gttgtaaaa tcaaccagca caaaagatgt ccagattaca 1980
tcattcagaa attgaacatt gtaaataaaa aagaaaaagc aactggaaga gaggtgactc 2040
acattcagth caccagctgg ccagaccacg ggggtgcctga ggatcctcac ttgctcctca 2100
aactgagaag gagagtgaat gccttcagca atttcttcag tgggtccatt gtggtgcact 2160

```

```

gcagtgtctgg tgttggggcgc acaggaacct atatcggaat tgatgccatg ctagaaggcc 2220
tggaagccga gaacaaagtg gatgtttatg gttatgttgt caagctaagg cgacagagat 2280
gcctgatggg tcaagtagag gccagtaga tcttgatcca tcaggctttg gtggaataca 2340
atcagtttgg agaaacagaa gtgaatttgt ctgaattaca tccatatcta cataacatga 2400
agaaaagggg tccacccagt gagccgtctc cactagaggg tgaattccag agacttcctt 2460
catataggag ctggaggaca cagcacattg gaaatcaaga agaaaataaa agtaaaaaca 2520
ggaattctaa tgtcatccca tatgactata acagagtggc acttaaacat gagctggaaa 2580
tgagtaaaga gagtgagcat gattcagatg aatcctctga tgatgacagt gattcagagg 2640
aaccaagcaa atacatcaat gcatctttta taatgagcta ctggaaacct gaagtgatga 2700
ttgctgtctc gggaccactg aaggagacca ttggtgactt ttggcagatg atcttccaaa 2760
gaaaagtcaa agttattgtt atgctgacag aactgaaaca tggagaccag gaaatctgtg 2820
ctcagtactg gggagaagga aagcaaocat atggagatat tgaagttgac ctgaaagaca 2880
cagacaaatc ttcaacttat acccttcgtg tctttgaact gagacattcc aagaggaaag 2940
actctcgaac tgtgtaccag taccaatata caaactggag tgtggagcag ctctctgcag 3000
aaccaagga attaatctct atgattcagg tcgtcaaaca aaaacttccc cagaagaatt 3060
cctctgaagg gaacaagcat cacaagagta cacctctact cattcactgc agggatggat 3120
ctcagcaaac gggaatatct tgtgctttgt taaatctctt agaaagtgcg gaaacagaag 3180
aggtagtggg tatttttcaa gtggtaaaag ctctacgcaa agctaggcca ggcattggtt 3240
ccacattcga gcaatatcaa ttcttatatg acgtcattgc cagcacctac cctgctcaga 3300
atggacaagt aaagaaaaac aaccatcaag aagataaaat tgaatttgat aatgaagtgg 3360
acaaagtaaa gcaggatgct aattgtgtta atccacttgg tgcccagaa aagctccctg 3420
aagcaaagga acaggctgaa ggttctgaac ccacgagtgg cactgagggg ccagaacatt 3480
ctgtcaatgg tcttgcaagt ccagctttaa atcaaggttc ataggaaaag acataaatga 3540
ggaaactcca aacctcctgt tagctgttat ttctattttt gtagaagtag gaagtgaaaa 3600
taggtataca gtggattaat taaatgcagc gaaccaatat ttgtagaagg gttatatatt 3660
actactgtgg aaaaatatatt aagatagttt tgccagaaca gtttgtacag acgtatgctt 3720
attttaaaat tttatctctt attcagtaaa aaacaacttc tttgtaatcg ttatgtgtgt 3780
atatgtatgt gtgtatgggt gtgtgtttgt gtgagagaca gagaaagaga gagaattctt 3840
tcaagtgaat ctaaaagctt ttgcttttcc tttgttttta tgaagaaaaa atacatttta 3900
tattagaagt gttaacttag cttgaaggat ctgtttttta aaatcataaa ctgtgtgcag 3960
actcaataaa atcatgtaca tttctgaaat gacctcaaga tgtcctcctt gttctactca 4020
tatatatcta tcttatatac ttactatttt acttctagag atagtacata aaggtgggat 4080
gtgtgtgtat gctactacaa aaaagttgtt aactaaatta acattgggaa atcttatatt 4140
ccatatatta gcatttagtc caatgtcttt ttaagcttat ttaattaaaa aatttccagt 4200
gagcttatca tgctgtcttt acatgggggt ttcaattttg catgctcgat tattccctgt 4260
acaatattta aaattttattg cttgatactt ttgacaacaa attaggtttt gtacaattga 4320
acttaaataa atgtcattaa aataaataaa tgcaatatgt attaatattc attgtataaa 4380
aatagaagaa tacaaacata tttgttaaat atttacatat gaaatttaat atagctattt 4440
ttatggaatt tttcattgat atgaaaaata tgatattgca tatgcatagt tcccatgtta 4500
aatcccattc ataactttca ttaaagcatt tactttgaat ttc 4543

```

<210> 101

<211> 1143

<212> PRT

<213> Homo sapiens

<400> 101

```

Met Tyr Leu Trp Leu Lys Leu Leu Ala Phe Gly Phe Ala Phe Leu Asp
 1           5           10           15
Thr Glu Val Phe Val Thr Gly Gln Ser Pro Thr Pro Ser Pro Thr Asp
          20           25           30
Ala Tyr Leu Asn Ala Ser Glu Thr Thr Leu Ser Pro Ser Gly Ser
          35           40           45
Ala Val Ile Ser Thr Thr Thr Ile Ala Thr Thr Pro Ser Lys Pro Thr
          50           55           60
Cys Asp Glu Lys Tyr Ala Asn Ile Thr Val Asp Tyr Leu Tyr Asn Lys
65           70           75           80
Glu Thr Lys Leu Phe Thr Ala Lys Leu Asn Val Asn Glu Asn Val Glu

```


				85					90					95			
Cys	Gly	Asn	Asn	Thr	Cys	Thr	Asn	Asn	Glu	Val	His	Asn	Leu	Thr	Glu		
			100					105					110				
Cys	Lys	Asn	Ala	Ser	Val	Ser	Ile	Ser	His	Asn	Ser	Cys	Thr	Ala	Pro		
		115					120					125					
Asp	Lys	Thr	Leu	Ile	Leu	Asp	Val	Pro	Pro	Gly	Val	Glu	Lys	Phe	Gln		
		130				135					140						
Leu	His	Asp	Cys	Thr	Gln	Val	Glu	Lys	Ala	Asp	Thr	Thr	Ile	Cys	Leu		
145					150					155					160		
Lys	Trp	Lys	Asn	Ile	Glu	Thr	Phe	Thr	Cys	Asp	Thr	Gln	Asn	Ile	Thr		
			165					170						175			
Tyr	Arg	Phe	Gln	Cys	Gly	Asn	Met	Ile	Phe	Asp	Asn	Lys	Glu	Ile	Lys		
			180					185					190				
Leu	Glu	Asn	Leu	Glu	Pro	Glu	His	Glu	Tyr	Lys	Cys	Asp	Ser	Glu	Ile		
		195					200					205					
Leu	Tyr	Asn	Asn	His	Lys	Phe	Thr	Asn	Ala	Ser	Lys	Ile	Ile	Lys	Thr		
		210				215					220						
Asp	Phe	Gly	Ser	Pro	Gly	Glu	Pro	Gln	Ile	Ile	Phe	Cys	Arg	Ser	Glu		
225					230					235					240		
Ala	Ala	His	Gln	Gly	Val	Ile	Thr	Trp	Asn	Pro	Pro	Gln	Arg	Ser	Phe		
			245					250					255				
His	Asn	Phe	Thr	Leu	Cys	Tyr	Ile	Lys	Glu	Thr	Glu	Lys	Asp	Cys	Leu		
			260					265					270				
Asn	Leu	Asp	Lys	Asn	Leu	Ile	Lys	Tyr	Asp	Leu	Gln	Asn	Leu	Lys	Pro		
		275					280					285					
Tyr	Thr	Lys	Tyr	Val	Leu	Ser	Leu	His	Ala	Tyr	Ile	Ile	Ala	Lys	Val		
		290				295					300						
Gln	Arg	Asn	Gly	Ser	Ala	Ala	Met	Cys	His	Phe	Thr	Thr	Lys	Ser	Ala		
305					310					315					320		
Pro	Pro	Ser	Gln	Val	Trp	Asn	Met	Thr	Val	Ser	Met	Thr	Ser	Asp	Asn		
			325					330						335			
Ser	Met	His	Val	Lys	Cys	Arg	Pro	Pro	Arg	Asp	Arg	Asn	Gly	Pro	His		
			340					345					350				
Glu	Arg	Tyr	His	Leu	Glu	Val	Glu	Ala	Gly	Asn	Thr	Leu	Val	Arg	Asn		
		355					360					365					
Glu	Ser	His	Lys	Asn	Cys	Asp	Phe	Arg	Val	Lys	Asp	Leu	Gln	Tyr	Ser		
		370				375					380						
Thr	Asp	Tyr	Thr	Phe	Lys	Ala	Tyr	Phe	His	Asn	Gly	Asp	Tyr	Pro	Gly		
385					390					395					400		
Glu	Pro	Phe	Ile	Leu	His	His	Ser	Thr	Ser	Tyr	Asn	Ser	Lys	Ala	Leu		
			405					410						415			
Ile	Ala	Phe	Leu	Ala	Phe	Leu	Ile	Ile	Val	Thr	Ser	Ile	Ala	Leu	Leu		
			420					425					430				
Val	Val	Leu	Tyr	Lys	Ile	Tyr	Asp	Leu	His	Lys	Lys	Arg	Ser	Cys	Asn		
		435					440					445					
Leu	Asp	Glu	Gln	Gln	Glu	Leu	Val	Glu	Arg	Asp	Asp	Glu	Lys	Gln	Leu		
		450				455					460						
Met	Asn	Val	Glu	Pro	Ile	His	Ala	Asp	Ile	Leu	Leu	Glu	Thr	Tyr	Lys		
465					470					475					480		
Arg	Lys	Ile	Ala	Asp	Glu	Gly	Arg	Leu	Phe	Leu	Ala	Glu	Phe	Gln	Ser		
			485					490						495			
Ile	Pro	Arg	Val	Phe	Ser	Lys	Phe	Pro	Ile	Lys	Glu	Ala	Arg	Lys	Pro		
			500					505					510				
Phe	Asn	Gln	Asn	Lys	Asn	Arg	Tyr	Val	Asp	Ile	Leu	Pro	Tyr	Asp	Tyr		
		515					520					525					
Asn	Arg	Val	Glu	Leu	Ser	Glu	Ile	Asn	Gly	Asp	Ala	Gly	Ser	Asn	Tyr		
		530				535					540						
Ile	Asn	Ala	Ser	Tyr	Ile	Asp	Gly	Phe	Lys	Glu	Pro	Arg	Lys	Tyr	Ile		

545		550		555		560									
Ala	Ala	Gln	Gly	Pro	Arg	Asp	Glu	Thr	Val	Asp	Asp	Phe	Trp	Arg	Met
				565					570					575	
Ile	Trp	Glu	Gln	Lys	Ala	Thr	Val	Ile	Val	Met	Val	Thr	Arg	Cys	Glu
			580					585					590		
Glu	Gly	Asn	Arg	Asn	Lys	Cys	Ala	Glu	Tyr	Trp	Pro	Ser	Met	Glu	Glu
		595					600					605			
Gly	Thr	Arg	Ala	Phe	Gly	Asp	Val	Val	Val	Lys	Ile	Asn	Gln	His	Lys
	610					615					620				
Arg	Cys	Pro	Asp	Tyr	Ile	Ile	Gln	Lys	Leu	Asn	Ile	Val	Asn	Lys	Lys
625					630					635				640	
Glu	Lys	Ala	Thr	Gly	Arg	Glu	Val	Thr	His	Ile	Gln	Phe	Thr	Ser	Trp
				645					650					655	
Pro	Asp	His	Gly	Val	Pro	Glu	Asp	Pro	His	Leu	Leu	Leu	Lys	Leu	Arg
			660					665					670		
Arg	Arg	Val	Asn	Ala	Phe	Ser	Asn	Phe	Phe	Ser	Gly	Pro	Ile	Val	Val
		675					680					685			
His	Cys	Ser	Ala	Gly	Val	Gly	Arg	Thr	Gly	Thr	Tyr	Ile	Gly	Ile	Asp
	690					695					700				
Ala	Met	Leu	Glu	Gly	Leu	Glu	Ala	Glu	Asn	Lys	Val	Asp	Val	Tyr	Gly
705					710					715				720	
Tyr	Val	Val	Lys	Leu	Arg	Arg	Gln	Arg	Cys	Leu	Met	Val	Gln	Val	Glu
				725					730					735	
Ala	Gln	Tyr	Ile	Leu	Ile	His	Gln	Ala	Leu	Val	Glu	Tyr	Asn	Gln	Phe
			740					745					750		
Gly	Glu	Thr	Glu	Val	Asn	Leu	Ser	Glu	Leu	His	Pro	Tyr	Leu	His	Asn
		755					760					765			
Met	Lys	Lys	Arg	Asp	Pro	Pro	Ser	Glu	Pro	Ser	Pro	Leu	Glu	Ala	Glu
	770					775					780				
Phe	Gln	Arg	Leu	Pro	Ser	Tyr	Arg	Ser	Trp	Arg	Thr	Gln	His	Ile	Gly
785					790					795				800	
Asn	Gln	Glu	Glu	Asn	Lys	Ser	Lys	Asn	Arg	Asn	Ser	Asn	Val	Ile	Pro
				805					810					815	
Tyr	Asp	Tyr	Asn	Arg	Val	Pro	Leu	Lys	His	Glu	Leu	Glu	Met	Ser	Lys
			820					825					830		
Glu	Ser	Glu	His	Asp	Ser	Asp	Glu	Ser	Ser	Asp	Asp	Asp	Ser	Asp	Ser
		835					840					845			
Glu	Glu	Pro	Ser	Lys	Tyr	Ile	Asn	Ala	Ser	Phe	Ile	Met	Ser	Tyr	Trp
	850					855					860				
Lys	Pro	Glu	Val	Met	Ile	Ala	Ala	Gln	Gly	Pro	Leu	Lys	Glu	Thr	Ile
865					870					875				880	
Gly	Asp	Phe	Trp	Gln	Met	Ile	Phe	Gln	Arg	Lys	Val	Lys	Val	Ile	Val
				885					890					895	
Met	Leu	Thr	Glu	Leu	Lys	His	Gly	Asp	Gln	Glu	Ile	Cys	Ala	Gln	Tyr
			900					905					910		
Trp	Gly	Glu	Gly	Lys	Gln	Thr	Tyr	Gly	Asp	Ile	Glu	Val	Asp	Leu	Lys
		915					920						925		
Asp	Thr	Asp	Lys	Ser	Ser	Thr	Tyr	Thr	Leu	Arg	Val	Phe	Glu	Leu	Arg
	930					935					940				
His	Ser	Lys	Arg	Lys	Asp	Ser	Arg	Thr	Val	Tyr	Gln	Tyr	Gln	Tyr	Thr
945					950					955				960	
Asn	Trp	Ser	Val	Glu	Gln	Leu	Pro	Ala	Glu	Pro	Lys	Glu	Leu	Ile	Ser
				965					970					975	
Met	Ile	Gln	Val	Val	Lys	Gln	Lys	Leu	Pro	Gln	Lys	Asn	Ser	Ser	Glu
			980					985					990		
Gly	Asn	Lys	His	His	Lys	Ser	Thr	Pro	Leu	Leu	Ile	His	Cys	Arg	Asp
		995					1000					1005			
Gly	Ser	Gln	Gln	Thr	Gly	Ile	Phe	Cys	Ala	Leu	Leu	Asn	Leu	Leu	Glu

1010	1015	1020
Ser Ala Glu Thr Glu Glu Val Val Asp Ile Phe Gln Val Val Lys Ala		
1025	1030	1035
Leu Arg Lys Ala Arg Pro Gly Met Val Ser Thr Phe Glu Gln Tyr Gln		1040
	1045	1050
Phe Leu Tyr Asp Val Ile Ala Ser Thr Tyr Pro Ala Gln Asn Gly Gln		1055
	1060	1065
Val Lys Lys Asn Asn His Gln Glu Asp Lys Ile Glu Phe Asp Asn Glu		1070
	1075	1080
Val Asp Lys Val Lys Gln Asp Ala Asn Cys Val Asn Pro Leu Gly Ala		1085
	1090	1095
Pro Glu Lys Leu Pro Glu Ala Lys Glu Gln Ala Glu Gly Ser Glu Pro		1100
	1105	1110
Thr Ser Gly Thr Glu Gly Pro Glu His Ser Val Asn Gly Pro Ala Ser		1115
	1125	1130
Pro Ala Leu Asn Gln Gly Ser		1135
	1140	

<210> 102
 <211> 5026
 <212> DNA
 <213> Homo sapiens

<400> 102

agaggaggaa	attgttcctc	gtctgataag	acaacagtgg	agaaaggacg	catgctgttt	60
cttagggaca	cggctgactt	ccagatatga	ccatgtattt	gtggcttaaa	ctcttggcat	120
ttggctttgc	ctttctggac	acagaagtat	ttgtgacagg	gcaaagccca	acaccttccc	180
ccactggatt	gactacagca	aagatgcccc	gtgttccact	ttcaagtgc	cccttaccta	240
ctcacaccac	tgcattctca	cccgaagca	cctttgaaag	agaaaatgac	ttctcagaga	300
ccacaacttc	tcttagtcca	gacaatactt	ccaccaagt	atccccggac	tctttggata	360
atgctagtgc	ttttaatacc	acaggtgttt	catcagtaca	gacgcctcac	cttcccacgc	420
acgcagactc	gcagacgccc	tctgctggaa	ctgacacgca	gacattcagc	ggctccgccg	480
ccaatgcaaa	actcaaccct	acccaggca	gcaatgctat	ctcagatgtc	ccaggagaga	540
ggagtacagc	cagcaccttt	cctacagacc	cagtttcccc	attgacaacc	accctcagcc	600
ttgcacacca	cagctctgct	gccttacctg	cacgcacctc	caacaccacc	atcacagcga	660
acacctcaga	tgcctacctt	aatgcctctg	aaacaaccac	tctgagccct	tctggaagcg	720
ctgtcatttc	aaccacaaca	atagctacta	ctccatctaa	gccaacatgt	gatgaaaaat	780
atgcaaacat	cactgtggat	tacttatata	acaaggaaac	taaattattt	acagcaaagc	840
taaagtgtaa	tgagaatgtg	gaatgtggaa	acaatacttg	cacaaacaat	gaggtgcata	900
accttacaga	atgtaaaaat	gcgtctgttt	ccatatctca	taattcatgt	actgctcctg	960
ataagacatt	aatattagat	gtgccaccag	gggttgaaaa	gtttcagtta	catgattgta	1020
cacaagttga	aaaagcagat	actactattt	gtttaaaatg	gaaaaatatt	gaaaccttta	1080
cttgtgatac	acagaatatt	acctacagat	ttcagtgtgg	taatatgata	tttgataata	1140
aagaaattaa	attagaaaac	cttgaacccg	aacatgagta	taagtgtgac	tcagaaatac	1200
tctataataa	ccacaagttt	actaacgcaa	gtaaaattat	taaaacagat	tttgggagtc	1260
caggagagcc	tcagattatt	ttttgtagaa	gtgaagctgc	acatcaagga	gtaattacct	1320
ggaatcccc	tcaaagatca	tttcataatt	ttaccctctg	ttatataaaa	gagacagaaa	1380
aagattgcct	caatctggat	aaaaacctga	tcaaatatga	tttgcaaaat	ttaaaacctt	1440
atacgaaata	tgttttatca	ttacatgcct	acatcattgc	aaaagtgcaa	cgtaatggaa	1500
gtgctgcaat	gtgtcatttc	acaactaaaa	gtgctcctcc	aagccaggtc	tggaacatga	1560
ctgtctccat	gacatcagat	aatagtatg	atgtcaagtg	taggcctccc	agggaccgta	1620
atggccccca	tgaacgttac	catttggaag	ttgaagcttg	aaatactctg	gttagaaattg	1680
agtcgcataa	gaattgcat	ttccgtgtaa	aagatcttca	atattcaaca	gactacactt	1740
ttaaggccta	ttttcacaat	ggagactatc	ctggagaacc	ctttatttta	catcattcaa	1800
catcttataa	ttctaaggca	ctgatagcat	ttctggcatt	tctgattatt	gtgacatcaa	1860
tagccctgct	tggtgttctc	tacaaaatct	atgatctaca	taagaaaaga	tcctgcaatt	1920
tagatgaaca	gcaggagctt	gttgaaaggg	atgatgaaaa	acaactgatg	aatgtggagc	1980

caatccatgc	agatatTTTTg	ttggaaaactt	ataagaggaa	gatttgctgat	gaaggaagac	2040
TTTTTctggc	tgaatttCag	agcatcccgC	gggtgttcag	caagtttCct	ataaaggaag	2100
ctcgaaagcc	ctttaaccag	aataaaaacc	gttatgttga	cattcttCct	tatgattata	2160
accgtgttga	actctctgag	ataaacggag	atgcagggtc	aaactacata	aatgccagct	2220
atattgatgg	tttcaaagaa	cccaggaaat	acattgctgc	acaaggTccc	agggatgaaa	2280
ctgttgatga	tttctggagg	atgatttggg	aacagaaagc	cacagttatt	gtcatggtca	2340
ctcgatgtga	agaaggaaac	aggaacaagt	gtgcagaata	ctggccgtca	atggaagagg	2400
gcactcgggc	TTTTggagat	gttgttgtaa	agatcaacca	gcacaaaaga	tgtccagatt	2460
acatcattca	gaaattgaac	attgtaaata	aaaaagaaaa	agcaactgga	agagaggtga	2520
ctcacattca	gttcaccagc	tggccagacc	acgggggtgc	tgaggatCct	cacttgctcc	2580
tcaaactgag	aaggagagtg	aatgccttca	gcaatttCct	cagtggTccc	attgtgggtgc	2640
actgcagtgc	tgggtgttggg	cgcacaggaa	cctatatcg	aattgatgcc	atgctagaag	2700
gcctggaagc	cgagaacaaa	gtggatgttt	atgggttatgt	tgtcaagcta	aggcgacaga	2760
gatgcctgat	ggttcaagta	gaggcccagt	acatcttgat	ccatcaggct	ttggtggaat	2820
acaatcagtt	tggagaaaca	gaagtgaatt	tgtctgaatt	acatccatat	ctacataaca	2880
tgaagaaaag	ggatccacc	agtgagccgt	ctccactaga	ggctgaattc	cagagacttc	2940
cttcatatag	gagctggagg	acacagcaca	ttggaaatca	agaagaaaat	aaaagtaaaa	3000
acaggaattc	taatgtcatc	ccatgatgact	ataacagagt	gccacttaaa	catgagctgg	3060
aaatgagtaa	agagagtga	catgattcag	atgaatCctc	tgatgatgac	agtgattcag	3120
aggaaccaag	caaatacatc	aatgcattct	ttataatgag	ctactggaaa	cctgaagtga	3180
tgattgctgc	tcagggacca	ctgaaggaga	ccattgggtga	cttttggcag	atgatcttcc	3240
aaagaaaagt	caaagttatt	gttatgctga	cagaactgaa	acatggagac	caggaaatct	3300
gtgctcagta	ctggggagaa	ggaaagcaaa	catatggaga	tattgaagtt	gacctgaaag	3360
acacagacaa	atcttcaact	tatacccttc	gtgtctttga	actgagacat	tccaagagga	3420
aagactctcg	aactgtgtac	cagtaccaat	atacaaactg	gagtgtggag	cagcttCctg	3480
cagaacccaa	ggaattaatc	tctatgattc	aggTcgtcaa	acaaaaactt	ccccagaaga	3540
attcctctga	agggaacaag	catcacaaga	gtacacctct	actcattcac	tgcagggatg	3600
gatctcagca	aacgggaata	ttttgtgctt	tgttaaactc	cttagaaagt	gcggaaacag	3660
aagaggtagt	ggatattttt	caagtggtaa	aagctctacg	caaagctagg	ccaggcatgg	3720
tttccacatt	cgagcaatat	caattcctat	atgacgtcat	tgccagcacc	taccctgctc	3780
agaatggaca	agtaaagaaa	aacaaccatc	aagaagataa	aattgaattt	gataatgaag	3840
tggacaaagt	aaagcaggat	gctaattgtg	ttaatccact	tggTgcccc	gaaaagctcc	3900
ctgaagcaaa	ggaacaggct	gaaggttctg	aaccacagag	tggcactgag	gggccagaac	3960
attctgtcaa	tggTcctgca	agTccagctt	taaatcaagg	ttcataggaa	aagacataaa	4020
tgaggaaact	ccaaacctcc	tgttagctgt	tatttctatt	tttgtagaag	taggaagtga	4080
aaataggtat	acagtggatt	aattaaatgc	agcgaacc	tatttgtaga	agggttatat	4140
tttactactg	tggaaaaata	tttaagatag	ttttgccaga	acagtttgta	cagacgtatg	4200
cttatttttaa	aattttatct	cttattcagt	aaaaaacaac	ttctttgtaa	tcgttatgtg	4260
tgtatatgta	tgtgtgtatg	ggtgtgtgtt	tgtgtgagag	acagagaaag	agagagaatt	4320
ctttcaagtg	aatctaaaag	cttttgcttt	tcctttgttt	ttatgaagaa	aaaatacatt	4380
ttatattaga	agtgttaact	tagcttgaag	gatctgtttt	taaaaatcat	aaactgtgtg	4440
cagactcaat	aaaatcatgt	acatttctga	aatgacctca	agatgtCctc	cttgttctac	4500
tcatatatat	ctatcttata	tacttactat	tttacttcta	gagatagtac	ataaagggtg	4560
tatgtgtgtg	tatgctacta	caaaaaagtt	gttaactaaa	ttacattgg	gaaatcttat	4620
attccataata	ttagcattta	gtccaatgtc	tttttaagct	tatttaatta	aaaaatttcc	4680
agtgagctta	tcatgctgtc	tttacaatgg	gttttcaatt	ttgcatgctc	gattattccc	4740
tgtacaatat	ttaaaattta	ttgcttgata	cttttgacaa	caaatttagt	tttgtacaat	4800
tgaacttaaa	taaatgtcat	taaaaataaat	aaatgcaata	tgtattaata	ttcattgtat	4860
aaaaatagaa	gaatacaaac	atattttgtta	aatattttaca	tatgaaattt	aatatagcta	4920
tttttatgga	atttttcatt	gatatgaaaa	atatgatatt	gcatatgcat	agttcccatg	4980
ttaaatccca	ttcataactt	tcattaaagc	atttactttg	aatttc		5026

<210> 103

<211> 1304

<212> PRT

<213> Homo sapiens

<400> 103

Met Tyr Leu Trp Leu Lys Leu Leu Ala Phe Gly Phe Ala Phe Leu Asp
 1 5 10 15
 Thr Glu Val Phe Val Thr Gly Gln Ser Pro Thr Pro Ser Pro Thr Gly
 20 25 30
 Leu Thr Thr Ala Lys Met Pro Ser Val Pro Leu Ser Ser Asp Pro Leu
 35 40 45
 Pro Thr His Thr Thr Ala Phe Ser Pro Ala Ser Thr Phe Glu Arg Glu
 50 55 60
 Asn Asp Phe Ser Glu Thr Thr Thr Ser Leu Ser Pro Asp Asn Thr Ser
 65 70 75 80
 Thr Gln Val Ser Pro Asp Ser Leu Asp Asn Ala Ser Ala Phe Asn Thr
 85 90 95
 Thr Gly Val Ser Ser Val Gln Thr Pro His Leu Pro Thr His Ala Asp
 100 105 110
 Ser Gln Thr Pro Ser Ala Gly Thr Asp Thr Gln Thr Phe Ser Gly Ser
 115 120 125
 Ala Ala Asn Ala Lys Leu Asn Pro Thr Pro Gly Ser Asn Ala Ile Ser
 130 135 140
 Asp Val Pro Gly Glu Arg Ser Thr Ala Ser Thr Phe Pro Thr Asp Pro
 145 150 155 160
 Val Ser Pro Leu Thr Thr Thr Leu Ser Leu Ala His His Ser Ser Ala
 165 170 175
 Ala Leu Pro Ala Arg Thr Ser Asn Thr Thr Ile Thr Ala Asn Thr Ser
 180 185 190
 Asp Ala Tyr Leu Asn Ala Ser Glu Thr Thr Thr Leu Ser Pro Ser Gly
 195 200 205
 Ser Ala Val Ile Ser Thr Thr Thr Ile Ala Thr Thr Pro Ser Lys Pro
 210 215 220
 Thr Cys Asp Glu Lys Tyr Ala Asn Ile Thr Val Asp Tyr Leu Tyr Asn
 225 230 235 240
 Lys Glu Thr Lys Leu Phe Thr Ala Lys Leu Asn Val Asn Glu Asn Val
 245 250 255
 Glu Cys Gly Asn Asn Thr Cys Thr Asn Asn Glu Val His Asn Leu Thr
 260 265 270
 Glu Cys Lys Asn Ala Ser Val Ser Ile Ser His Asn Ser Cys Thr Ala
 275 280 285
 Pro Asp Lys Thr Leu Ile Leu Asp Val Pro Pro Gly Val Glu Lys Phe
 290 295 300
 Gln Leu His Asp Cys Thr Gln Val Glu Lys Ala Asp Thr Thr Ile Cys
 305 310 315 320
 Leu Lys Trp Lys Asn Ile Glu Thr Phe Thr Cys Asp Thr Gln Asn Ile
 325 330 335
 Thr Tyr Arg Phe Gln Cys Gly Asn Met Ile Phe Asp Asn Lys Glu Ile
 340 345 350
 Lys Leu Glu Asn Leu Glu Pro Glu His Glu Tyr Lys Cys Asp Ser Glu
 355 360 365
 Ile Leu Tyr Asn Asn His Lys Phe Thr Asn Ala Ser Lys Ile Ile Lys
 370 375 380
 Thr Asp Phe Gly Ser Pro Gly Glu Pro Gln Ile Ile Phe Cys Arg Ser
 385 390 395 400
 Glu Ala Ala His Gln Gly Val Ile Thr Trp Asn Pro Pro Gln Arg Ser
 405 410 415
 Phe His Asn Phe Thr Leu Cys Tyr Ile Lys Glu Thr Glu Lys Asp Cys
 420 425 430
 Leu Asn Leu Asp Lys Asn Leu Ile Lys Tyr Asp Leu Gln Asn Leu Lys
 435 440 445

Pro Tyr Thr Lys Tyr Val Leu Ser Leu His Ala Tyr Ile Ile Ala Lys
 450 455 460
 Val Gln Arg Asn Gly Ser Ala Ala Met Cys His Phe Thr Thr Lys Ser
 465 470 475 480
 Ala Pro Pro Ser Gln Val Trp Asn Met Thr Val Ser Met Thr Ser Asp
 485 490 495
 Asn Ser Met His Val Lys Cys Arg Pro Pro Arg Asp Arg Asn Gly Pro
 500 505 510
 His Glu Arg Tyr His Leu Glu Val Glu Ala Gly Asn Thr Leu Val Arg
 515 520 525
 Asn Glu Ser His Lys Asn Cys Asp Phe Arg Val Lys Asp Leu Gln Tyr
 530 535 540
 Ser Thr Asp Tyr Thr Phe Lys Ala Tyr Phe His Asn Gly Asp Tyr Pro
 545 550 555 560
 Gly Glu Pro Phe Ile Leu His His Ser Thr Ser Tyr Asn Ser Lys Ala
 565 570 575
 Leu Ile Ala Phe Leu Ala Phe Leu Ile Ile Val Thr Ser Ile Ala Leu
 580 585 590
 Leu Val Val Leu Tyr Lys Ile Tyr Asp Leu His Lys Lys Arg Ser Cys
 595 600 605
 Asn Leu Asp Glu Gln Gln Glu Leu Val Glu Arg Asp Asp Glu Lys Gln
 610 615 620
 Leu Met Asn Val Glu Pro Ile His Ala Asp Ile Leu Leu Glu Thr Tyr
 625 630 635 640
 Lys Arg Lys Ile Ala Asp Glu Gly Arg Leu Phe Leu Ala Glu Phe Gln
 645 650 655
 Ser Ile Pro Arg Val Phe Ser Lys Phe Pro Ile Lys Glu Ala Arg Lys
 660 665 670
 Pro Phe Asn Gln Asn Lys Asn Arg Tyr Val Asp Ile Leu Pro Tyr Asp
 675 680 685
 Tyr Asn Arg Val Glu Leu Ser Glu Ile Asn Gly Asp Ala Gly Ser Asn
 690 695 700
 Tyr Ile Asn Ala Ser Tyr Ile Asp Gly Phe Lys Glu Pro Arg Lys Tyr
 705 710 715 720
 Ile Ala Ala Gln Gly Pro Arg Asp Glu Thr Val Asp Asp Phe Trp Arg
 725 730 735
 Met Ile Trp Glu Gln Lys Ala Thr Val Ile Val Met Val Thr Arg Cys
 740 745 750
 Glu Glu Gly Asn Arg Asn Lys Cys Ala Glu Tyr Trp Pro Ser Met Glu
 755 760 765
 Glu Gly Thr Arg Ala Phe Gly Asp Val Val Val Lys Ile Asn Gln His
 770 775 780
 Lys Arg Cys Pro Asp Tyr Ile Ile Gln Lys Leu Asn Ile Val Asn Lys
 785 790 795 800
 Lys Glu Lys Ala Thr Gly Arg Glu Val Thr His Ile Gln Phe Thr Ser
 805 810 815
 Trp Pro Asp His Gly Val Pro Glu Asp Pro His Leu Leu Leu Lys Leu
 820 825 830
 Arg Arg Arg Val Asn Ala Phe Ser Asn Phe Phe Ser Gly Pro Ile Val
 835 840 845
 Val His Cys Ser Ala Gly Val Gly Arg Thr Gly Thr Tyr Ile Gly Ile
 850 855 860
 Asp Ala Met Leu Glu Gly Leu Glu Ala Glu Asn Lys Val Asp Val Tyr
 865 870 875 880
 Gly Tyr Val Val Lys Leu Arg Arg Gln Arg Cys Leu Met Val Gln Val
 885 890 895
 Glu Ala Gln Tyr Ile Leu Ile His Gln Ala Leu Val Glu Tyr Asn Gln
 900 905 910

Phe Gly Glu Thr Glu Val Asn Leu Ser Glu Leu His Pro Tyr Leu His
 915 920 925
 Asn Met Lys Lys Arg Asp Pro Pro Ser Glu Pro Ser Pro Leu Glu Ala
 930 935 940
 Glu Phe Gln Arg Leu Pro Ser Tyr Arg Ser Trp Arg Thr Gln His Ile
 945 950 955 960
 Gly Asn Gln Glu Glu Asn Lys Ser Lys Asn Arg Asn Ser Asn Val Ile
 965 970 975
 Pro Tyr Asp Tyr Asn Arg Val Pro Leu Lys His Glu Leu Glu Met Ser
 980 985 990
 Lys Glu Ser Glu His Asp Ser Asp Glu Ser Ser Asp Asp Asp Ser Asp
 995 1000 1005
 Ser Glu Glu Pro Ser Lys Tyr Ile Asn Ala Ser Phe Ile Met Ser Tyr
 1010 1015 1020
 Trp Lys Pro Glu Val Met Ile Ala Ala Gln Gly Pro Leu Lys Glu Thr
 1025 1030 1035 1040
 Ile Gly Asp Phe Trp Gln Met Ile Phe Gln Arg Lys Val Lys Val Ile
 1045 1050 1055
 Val Met Leu Thr Glu Leu Lys His Gly Asp Gln Glu Ile Cys Ala Gln
 1060 1065 1070
 Tyr Trp Gly Glu Gly Lys Gln Thr Tyr Gly Asp Ile Glu Val Asp Leu
 1075 1080 1085
 Lys Asp Thr Asp Lys Ser Ser Thr Tyr Thr Leu Arg Val Phe Glu Leu
 1090 1095 1100
 Arg His Ser Lys Arg Lys Asp Ser Arg Thr Val Tyr Gln Tyr Gln Tyr
 1105 1110 1115 1120
 Thr Asn Trp Ser Val Glu Gln Leu Pro Ala Glu Pro Lys Glu Leu Ile
 1125 1130 1135
 Ser Met Ile Gln Val Val Lys Gln Lys Leu Pro Gln Lys Asn Ser Ser
 1140 1145 1150
 Glu Gly Asn Lys His His Lys Ser Thr Pro Leu Leu Ile His Cys Arg
 1155 1160 1165
 Asp Gly Ser Gln Gln Thr Gly Ile Phe Cys Ala Leu Leu Asn Leu Leu
 1170 1175 1180
 Glu Ser Ala Glu Thr Glu Glu Val Val Asp Ile Phe Gln Val Val Lys
 1185 1190 1195 1200
 Ala Leu Arg Lys Ala Arg Pro Gly Met Val Ser Thr Phe Glu Gln Tyr
 1205 1210 1215
 Gln Phe Leu Tyr Asp Val Ile Ala Ser Thr Tyr Pro Ala Gln Asn Gly
 1220 1225 1230
 Gln Val Lys Lys Asn Asn His Gln Glu Asp Lys Ile Glu Phe Asp Asn
 1235 1240 1245
 Glu Val Asp Lys Val Lys Gln Asp Ala Asn Cys Val Asn Pro Leu Gly
 1250 1255 1260
 Ala Pro Glu Lys Leu Pro Glu Ala Lys Glu Gln Ala Glu Gly Ser Glu
 1265 1270 1275 1280
 Pro Thr Ser Gly Thr Glu Gly Pro Glu His Ser Val Asn Gly Pro Ala
 1285 1290 1295
 Ser Pro Ala Leu Asn Gln Gly Ser
 1300

<210> 104

<211> 1045

<212> DNA

<213> Homo sapiens

<400> 104

```

agaggaggaa attgttcctc gtctgataag acaacagtgg agaaaggacg catgctgttt 60
cttagggaca cggctgactt ccagatatga ccatgtattt gtggcttaaa ctcttggcat 120
ttggctttgc ctttctggac acagaagtat ttgtgacagg gcaaagccca acaccttccc 180
ccactggtaa gaattaatat ttatatTTTT actaatttta ttttcttggt gcaaagttaa 240
tatatttaac tacaattttc tattattaac actgaaatta tttttaagga taaattttat 300
aatcatgagt gattcttgac attcacttgt tcttaaactt tctgcttata cgttatagag 360
tttaataact acctaaacat gttattaaat ttgtatatat attttgtgta taaatagtaa 420
cttttcccaa acttgacagt aaatcacaca acagggtttct actctctttt aatattttta 480
gactataaaa aaatgcattt aaattagata acaaaatttt atagtctgaa agcagggttaa 540
cagctgtcta tgtatgttat agatatgtag ataacagatt tgcataatgta tatattttct 600
taagagtatg ttgctttttt cagtgggtatg caaaaccttt gagactattg agatattttt 660
aaataataat tttcaaattc tactgaacac ttcaatagtc cttataaatg tcttaatcat 720
gagataaatt taaaacacag agatgctgca aataaattca tacatagtag atacaaaata 780
agagaaaaaa tttaattgca gatgggttaa tatcacatca cttaactgat gttactgaaa 840
atgtattttc ctgcataatc atatgggtga cagtatgcat taagaaggta agtaaaacaa 900
tgaagacaat tttgatttaa tatggtaatg cacaattcca actaacgtac attcaacaga 960
tcatgaaatt gggttattaa aatgaatatt tttgtcatta aataaaaatt ccgtccaaaa 1020
aaaaaaaaaa aaaaaaaaaa aaaaaa

```

1045

<210> 105

<211> 34

<212> PRT

<213> Homo sapiens

<400> 105

```

Met Tyr Leu Trp Leu Lys Leu Leu Ala Phe Gly Phe Ala Phe Leu Asp
 1           5           10           15
Thr Glu Val Phe Val Thr Gly Gln Ser Pro Thr Pro Ser Pro Thr Gly
          20           25           30
Lys Asn

```

<210> 106

<211> 11

<212> PRT

<213> Unknown

<220>

<223> Conserved amino acids that may be found at
positions in a PTP polypeptide

<221> VARIANT

<222> 1

<223> Xaa = Ile or Val

<221> VARIANT

<222> 4, 7, 8

<223> Xaa = Any Amino Acid

<221> VARIANT

<222> 10

<223> Xaa = Ser or Thr

<400> 106

```

Xaa His Cys Xaa Ala Gly Xaa Xaa Arg Xaa Gly
 1           5           10

```


<210> 107
<211> 8
<212> PRT
<213> Unknown

<220>
<223> Catalytic cysteine motif

<221> VARIANT
<222> 2, 3, 4, 5, 6
<223> Xaa = Any Amino Acid

<221> VARIANT
<222> 8
<223> Xaa = Ser or Thr

<400> 107
Cys Xaa Xaa Xaa Xaa Xaa Arg Xaa
1 5

<210> 108
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Amino acids 1170-1176 of the EGF receptor sequence
(fluorescently-labeled) may be substrates for
acalytically active PTPs.

<400> 108
Asn Ala Glu Tyr Leu Arg Val
1 5

<210> 109
<211> 7
<212> PRT
<213> Unknown

<220>
<223> Catalytic cysteine motif sequence

<221> VARIANT
<222> 3, 4, 5, 6
<223> Xaa = Any Amino Acid

<400> 109
Cys Ser Xaa Xaa Xaa Xaa Arg
1 5

<210> 110
<211> 435
<212> PRT
<213> Unknown

<220>

<223> PTP1B mutant sequence

<400> 110

```

Met Glu Met Glu Lys Glu Phe Glu Gln Ile Asp Lys Ser Gly Ser Trp
 1           5           10           15
Ala Ala Ile Tyr Gln Asp Ile Arg His Glu Ala Ser Asp Phe Pro Cys
 20           25           30
Arg Val Ala Lys Leu Pro Lys Asn Lys Asn Arg Asn Arg Tyr Arg Asp
 35           40           45
Val Ser Pro Phe Asp His Ser Arg Ile Lys Leu His Gln Glu Asp Asn
 50           55           60
Asp Tyr Ile Asn Ala Ser Leu Ile Lys Met Glu Glu Ala Gln Arg Ser
 65           70           75           80
Tyr Ile Leu Thr Gln Gly Pro Leu Pro Asn Thr Cys Gly His Phe Trp
 85           90           95
Glu Met Val Trp Glu Gln Lys Ser Arg Gly Val Val Met Leu Asn Arg
100           105           110
Val Met Glu Lys Gly Ser Leu Lys Cys Ala Gln Tyr Trp Pro Gln Lys
115           120           125
Glu Glu Lys Glu Met Ile Phe Glu Asp Thr Asn Leu Lys Leu Thr Leu
130           135           140
Ile Ser Glu Asp Ile Lys Ser Tyr Tyr Thr Val Arg Gln Leu Glu Leu
145           150           155           160
Glu Asn Leu Thr Thr Gln Glu Thr Arg Glu Ile Leu His Phe His Tyr
165           170           175
Thr Thr Trp Pro Asp Phe Gly Val Pro Glu Ser Pro Ala Ser Phe Leu
180           185           190
Asn Phe Leu Phe Lys Val Arg Glu Ser Gly Ser Leu Ser Pro Glu His
195           200           205
Gly Pro Val Val Val His Ala Ala Gly Ile Gly Arg Ser Gly Thr
210           215           220
Phe Cys Leu Ala Asp Thr Cys Leu Leu Leu Met Asp Lys Arg Lys Asp
225           230           235           240
Pro Ser Ser Val Asp Ile Lys Lys Val Leu Leu Glu Met Arg Lys Phe
245           250           255
Arg Met Gly Leu Ile Gln Thr Ala Asp Gln Leu Arg Phe Ser Tyr Leu
260           265           270
Ala Val Ile Glu Gly Ala Lys Phe Ile Met Gly Asp Ser Ser Val Gln
275           280           285
Asp Gln Trp Lys Glu Leu Ser His Glu Asp Leu Glu Pro Pro Pro Glu
290           295           300
His Ile Pro Pro Pro Arg Pro Pro Lys Arg Ile Leu Glu Pro His
305           310           315           320
Asn Gly Lys Cys Arg Glu Phe Phe Pro Asn His Gln Trp Val Lys Glu
325           330           335
Glu Thr Gln Glu Asp Lys Asp Cys Pro Ile Lys Glu Glu Lys Gly Ser
340           345           350
Pro Leu Asn Ala Ala Pro Tyr Gly Ile Glu Ser Met Ser Gln Asp Thr
355           360           365
Glu Val Arg Ser Arg Val Val Gly Gly Ser Leu Arg Gly Ala Gln Ala
370           375           380
Ala Ser Pro Ala Lys Gly Glu Pro Ser Leu Pro Glu Lys Asp Glu Asp
385           390           395           400
His Ala Leu Ser Tyr Trp Lys Pro Phe Leu Val Asn Met Cys Val Ala
405           410           415
Thr Val Leu Thr Ala Gly Ala Tyr Leu Cys Tyr Arg Phe Leu Phe Asn

```

Ser Asn Thr
435

425

430

<210> 111
<211> 435
<212> PRT
<213> unknown

<220>

<223> PTP1B mutant sequence

<400> 111

Met	Glu	Met	Glu	Lys	Glu	Phe	Glu	Gln	Ile	Asp	Lys	Ser	Gly	Ser	Trp
1				5					10					15	
Ala	Ala	Ile	Tyr	Gln	Asp	Ile	Arg	His	Glu	Ala	Ser	Asp	Phe	Pro	Cys
			20					25					30		
Arg	Val	Ala	Lys	Leu	Pro	Lys	Asn	Lys	Asn	Arg	Asn	Arg	Tyr	Arg	Asp
		35					40					45			
Val	Ser	Pro	Phe	Asp	His	Ser	Arg	Ile	Lys	Leu	His	Gln	Glu	Asp	Asn
	50					55					60				
Asp	Tyr	Ile	Asn	Ala	Ser	Leu	Ile	Lys	Met	Glu	Glu	Ala	Gln	Arg	Ser
65				70					75					80	
Tyr	Ile	Leu	Thr	Gln	Gly	Pro	Leu	Pro	Asn	Thr	Cys	Gly	His	Phe	Trp
			85					90					95		
Glu	Met	Val	Trp	Glu	Gln	Lys	Ser	Arg	Gly	Val	Val	Met	Leu	Asn	Arg
			100					105					110		
Val	Met	Glu	Lys	Gly	Ser	Leu	Lys	Cys	Ala	Gln	Tyr	Trp	Pro	Gln	Lys
	115						120					125			
Glu	Glu	Lys	Glu	Met	Ile	Phe	Glu	Asp	Thr	Asn	Leu	Lys	Leu	Thr	Leu
	130					135					140				
Ile	Ser	Glu	Asp	Ile	Lys	Ser	Tyr	Tyr	Thr	Val	Arg	Gln	Leu	Glu	Leu
145					150					155					160
Glu	Asn	Leu	Thr	Thr	Gln	Glu	Thr	Arg	Glu	Ile	Leu	His	Phe	His	Tyr
				165				170						175	
Thr	Thr	Trp	Pro	Asp	Phe	Gly	Val	Pro	Glu	Ser	Pro	Ala	Ser	Phe	Leu
			180					185					190		
Asn	Phe	Leu	Phe	Lys	Val	Arg	Glu	Ser	Gly	Ser	Leu	Ser	Pro	Glu	His
	195						200					205			
Gly	Pro	Val	Val	Val	His	Ser	Ala	Ala	Gly	Ile	Gly	Arg	Ser	Gly	Thr
	210					215					220				
Phe	Cys	Leu	Ala	Asp	Thr	Cys	Leu	Leu	Leu	Met	Asp	Lys	Arg	Lys	Asp
225					230					235					240
Pro	Ser	Ser	Val	Asp	Ile	Lys	Lys	Val	Leu	Leu	Glu	Met	Arg	Lys	Phe
				245					250					255	
Arg	Met	Gly	Leu	Ile	Gln	Thr	Ala	Asp	Gln	Leu	Arg	Phe	Ser	Tyr	Leu
			260					265					270		
Ala	Val	Ile	Glu	Gly	Ala	Lys	Phe	Ile	Met	Gly	Asp	Ser	Ser	Val	Gln
		275					280					285			
Asp	Gln	Trp	Lys	Glu	Leu	Ser	His	Glu	Asp	Leu	Glu	Pro	Pro	Pro	Glu
	290					295					300				
His	Ile	Pro	Pro	Pro	Pro	Arg	Pro	Pro	Lys	Arg	Ile	Leu	Glu	Pro	His
305					310					315					320
Asn	Gly	Lys	Cys	Arg	Glu	Phe	Phe	Pro	Asn	His	Gln	Trp	Val	Lys	Glu
				325					330					335	
Glu	Thr	Gln	Glu	Asp	Lys	Asp	Cys	Pro	Ile	Lys	Glu	Glu	Lys	Gly	Ser
			340					345						350	

Pro Leu Asn Ala Ala Pro Tyr Gly Ile Glu Ser Met Ser Gln Asp Thr
 355 360 365
 Glu Val Arg Ser Arg Val Val Gly Gly Ser Leu Arg Gly Ala Gln Ala
 370 375 380
 Ala Ser Pro Ala Lys Gly Glu Pro Ser Leu Pro Glu Lys Asp Glu Asp
 385 390 395 400
 His Ala Leu Ser Tyr Trp Lys Pro Phe Leu Val Asn Met Cys Val Ala
 405 410 415
 Thr Val Leu Thr Ala Gly Ala Tyr Leu Cys Tyr Arg Phe Leu Phe Asn
 420 425 430
 Ser Asn Thr
 435

<210> 112
 <211> 1087
 <212> DNA
 <213> Homo sapiens

<400> 112
 acattgcatc cctgggataa acggacctgg acaactcact ctcttgggtct gtggctgctg 60
 cggttacctg gatgggcgaa cacctctgag gctggctttg ttacctgggc aataaggac 120
 tagcagttca gccgttttct atgcctgctg gatttggttg tatttggtcc cagccactgc 180
 tcatgtaatg tactccctta accaggaaat taaagcattc tcccgggaata atctcaggaa 240
 gcaatgcacc aggggtgacaa cgctaactgg aaagaaaatt atagaaacat ggaaagatgc 300
 cagaattcat gttgtggaag aagtagagcc gagcagtggg ggtgggtgtg gttatgtgca 360
 ggaccttagc tcggacctgc aagttggcgt tattaagcca tggttgctcc tagggtcaca 420
 agatgctgct catgatttgg atacactgaa aaagaataag gtgactcata ttcttaatgt 480
 tgcataatgga gttgaaaatg ctttcctcag tgactttaca tataagagca tttctatatt 540
 ggatctgcct gaaaccaaca tcctgtctta tttccagaa tgttttgaat ttattgaaga 600
 agcaaaaaga aaagatggag tggttcttgt tcattgtaat gcaggcggtt ccagggtgctgc 660
 tgcaattgta ataggtttcc tgatgaattc tgaacaaacc tcatttacca gtgctttttc 720
 tttggtgaaa aatgcaagac cttccatatg tccaaattct ggcttcattg agcagcttcg 780
 tacatatcaa gagggcaag aaagcaataa gtgtgacaga atacaggaga acagttcatg 840
 agttgcattg tagcagacaa tggacaactg tagtttctga attgacttct atagccatcg 900
 tttccctttt ttggagagta gactagcaaa actccctttt ttctcttgcc ttttttatgc 960
 ataaatggag gtcaatctga ttgtcctgac ctactgtata agtaaatctt aaatgtcatt 1020
 actttctctt tgttattata atgtgtgatt aaatgctttt ttaaattgct aagggaaaat 1080
 aaaaaaa 1087

<210> 113
 <211> 217
 <212> PRT
 <213> Homo sapiens

<400> 113
 Met Tyr Ser Leu Asn Gln Glu Ile Lys Ala Phe Ser Arg Asn Asn Leu
 1 5 10 15
 Arg Lys Gln Cys Thr Arg Val Thr Thr Leu Thr Gly Lys Lys Ile Ile
 20 25 30
 Glu Thr Trp Lys Asp Ala Arg Ile His Val Val Glu Glu Val Glu Pro
 35 40 45
 Ser Ser Gly Gly Gly Cys Gly Tyr Val Gln Asp Leu Ser Ser Asp Leu
 50 55 60
 Gln Val Gly Val Ile Lys Pro Trp Leu Leu Leu Gly Ser Gln Asp Ala
 65 70 75 80
 Ala His Asp Leu Asp Thr Leu Lys Lys Asn Lys Val Thr His Ile Leu
 85 90 95

```
<210> 114
<211> 1106
<212> DNA
<213> Homo sapiens
```

gacgcgtggc	catgttggag	gctccggggc	cgagtgatgg	ctgcgagctc	agcaacccca	60
gcgccagcag	agtcagctgt	gccggggcaga	tgctggaagt	gcagccagga	ttgtatttcg	120
gtggggccgc	ggccgtcgcg	gagccagatc	acctgagggg	agcgggcata	acggccgtgc	180
taacagtgga	ctcggaggag	cccagcttca	aggcggggcc	tggggctcgag	gatctatggc	240
gcctcttcgt	gccagcgctg	gacaaacccg	agacggacct	actcagccat	ctggaccggg	300
gcgtggccct	catcggtcag	gcccgcgctg	agggccgtgc	gggtgttggtg	cactgtcatg	360
caggagtcag	togaagtgtg	gccataataa	ctgcttttct	catgaagact	gaccaacttc	420
cctttgaaaa	agcctatgaa	aagctccaga	ttctcaaacc	agaggctaag	atgaatgagg	480
ggtttgagtg	gcaactgaaa	ttataaccagg	caatgggata	cgaagtggat	acctctagt	540
caatttataa	gcaatatcgt	ttacaaaagg	ttacagagaa	gtatccagaa	ttgcagaatt	600
tacctcaaga	actctttgct	gttgacccaa	ctaccgttct	acaaggattg	aaagatgagg	660
ttctctacaa	gtgtagaaa	tgcaggcgat	cattatttcg	aagttctagt	attctggatc	720
accgtgaagg	aagttggacct	atagcctttg	cccacaagag	aatgacacca	tcttccatgc	780
ttaccacagg	gaggcaagct	caatgtacat	cttatttcat	tgaacctgta	cagtggatgg	840
aatctgcttt	gttgggagt	atggatggac	agcttcttgg	cccaaaatgc	agtccaagt	900
tgggttcctt	caactgggat	gggtgaacagt	gctcttcttg	taggtggata	acacctgctt	960
ttcaaataca	taagaataga	gtggatgaaa	tgaaaatatt	gcctgttttg	ggatcacaaa	1020
caggaaaaat	atgaacatga	tattttatag	cttgggaaga	aacttgcaga	tgatatgtgc	1080
tgcccttgct	tcttatcatt	catggc				1106

```
<210> 115
<211> 340
<212> PRT
<213> Homo sapiens
```

Met	Leu	Glu	Ala	Pro	Gly	Pro	Ser	Asp	Gly	Cys	Glu	Leu	Ser	Asn	Pro
1				5					10					15	
Ser	Ala	Ser	Arg	Val	Ser	Cys	Ala	Gly	Gln	Met	Leu	Glu	Val	Gln	Pro
			20					25					30		
Gly	Leu	Tyr	Phe	Gly	Gly	Ala	Ala	Ala	Val	Ala	Glu	Pro	Asp	His	Leu
		35				40						45			
Arg	Glu	Ala	Gly	Ile	Thr	Ala	Val	Leu	Thr	Val	Asp	Ser	Glu	Glu	Pro
	50					55					60				

Ser Phe Lys Ala Gly Pro Gly Val Glu Asp Leu Trp Arg Leu Phe Val
 65 70 75 80
 Pro Ala Leu Asp Lys Pro Glu Thr Asp Leu Leu Ser His Leu Asp Arg
 85 90 95
 Cys Val Ala Phe Ile Gly Gln Ala Arg Ala Glu Gly Arg Ala Val Leu
 100 105 110
 Val His Cys His Ala Gly Val Ser Arg Ser Val Ala Ile Ile Thr Ala
 115 120 125
 Phe Leu Met Lys Thr Asp Gln Leu Pro Phe Glu Lys Ala Tyr Glu Lys
 130 135 140
 Leu Gln Ile Leu Lys Pro Glu Ala Lys Met Asn Glu Gly Phe Glu Trp
 145 150 155 160
 Gln Leu Lys Leu Tyr Gln Ala Met Gly Tyr Glu Val Asp Thr Ser Ser
 165 170 175
 Ala Ile Tyr Lys Gln Tyr Arg Leu Gln Lys Val Thr Glu Lys Tyr Pro
 180 185 190
 Glu Leu Gln Asn Leu Pro Gln Glu Leu Phe Ala Val Asp Pro Thr Thr
 195 200 205
 Val Ser Gln Gly Leu Lys Asp Glu Val Leu Tyr Lys Cys Arg Lys Cys
 210 215 220
 Arg Arg Ser Leu Phe Arg Ser Ser Ser Ile Leu Asp His Arg Glu Gly
 225 230 235 240
 Ser Gly Pro Ile Ala Phe Ala His Lys Arg Met Thr Pro Ser Ser Met
 245 250 255
 Leu Thr Thr Gly Arg Gln Ala Gln Cys Thr Ser Tyr Phe Ile Glu Pro
 260 265 270
 Val Gln Trp Met Glu Ser Ala Leu Leu Gly Val Met Asp Gly Gln Leu
 275 280 285
 Leu Cys Pro Lys Cys Ser Ala Lys Leu Gly Ser Phe Asn Trp Tyr Gly
 290 295 300
 Glu Gln Cys Ser Cys Gly Arg Trp Ile Thr Pro Ala Phe Gln Ile His
 305 310 315 320
 Lys Asn Arg Val Asp Glu Met Lys Ile Leu Pro Val Leu Gly Ser Gln
 325 330 335
 Thr Gly Lys Ile
 340

<210> 116

<211> 1017

<212> DNA

<213> Homo sapiens

<400> 116

gacgcgtggc catgttggag gctccggggc cgagtgatgg ctgcgagctc agcaacccca 60
 gcgccagcag agtcagctgt gccgggcaga tgctggaagt gcagccagga ttgtatttcg 120
 gtggggccgc ggccgtcgcg gagccagatc acctgaggga agcgggcatc acggccgtgc 180
 taacagtgga ctcgaggagag cccagcttca aggcggggcc tggggtcgag gatctatggc 240
 gcctcttcgt gccagcgctg gacaaacccg agacggacct actcagccat ctggaccggt 300
 gcgtggcctt catcggtcag gccgcgctg agggccgtgc ggtgttggtg cactgtcatg 360
 caggagtcag tcgaagtgtg gccataataa ctgcttttct catgaagact gaccaacttc 420
 cctttgaaa agcctatgaa aagctccaga ttctcaaacc agaggctaag atgaatgagg 480
 gggttgagt gcaactgaaa ttataaccagg caatgggata cgaagtggat acctctagtg 540
 caatttataa gcaatatcgt ttacaaaagg ttacagagaa gtatccagaa ttgcagaatt 600
 tacctcaaga actctttgct gttgacccaa ctaccgtttc acaaggattg aaagatgagg 660
 ttctctacaa gtgtagaaag tgcaggcgat cattatttcg aagttctagt attctggatc 720
 accgtgaagg aagtggacct atagcctttg ccacaaagag aatgacacca tcttccatgc 780
 ttaccacagg gaggcaagct caatgtacat cttatttcat tgaacctgta cagtggatgg 840

aatctgctttt gttgggagtg atggatggac aggtgagaac acattttatt ttctacaatt 900
 ttattttatg atctatatatt tattccttct tgcattttta gctctatttt aactagtgtt 960
 ttgctccatt tcttaatttc tttatttctg atgattatat ctttcttgtag tagataa 1017

<210> 117
 <211> 299
 <212> PRT
 <213> Homo sapiens

<400> 117
 Met Leu Glu Ala Pro Gly Pro Ser Asp Gly Cys Glu Leu Ser Asn Pro
 1 5 10 15
 Ser Ala Ser Arg Val Ser Cys Ala Gly Gln Met Leu Glu Val Gln Pro
 20 25 30
 Gly Leu Tyr Phe Gly Gly Ala Ala Val Ala Glu Pro Asp His Leu
 35 40 45
 Arg Glu Ala Gly Ile Thr Ala Val Leu Thr Val Asp Ser Glu Glu Pro
 50 55 60
 Ser Phe Lys Ala Gly Pro Gly Val Glu Asp Leu Trp Arg Leu Phe Val
 65 70 75 80
 Pro Ala Leu Asp Lys Pro Glu Thr Asp Leu Leu Ser His Leu Asp Arg
 85 90 95
 Cys Val Ala Phe Ile Gly Gln Ala Arg Ala Glu Gly Arg Ala Val Leu
 100 105 110
 Val His Cys His Ala Gly Val Ser Arg Ser Val Ala Ile Ile Thr Ala
 115 120 125
 Phe Leu Met Lys Thr Asp Gln Leu Pro Phe Glu Lys Ala Tyr Glu Lys
 130 135 140
 Leu Gln Ile Leu Lys Pro Glu Ala Lys Met Asn Glu Gly Phe Glu Trp
 145 150 155 160
 Gln Leu Lys Leu Tyr Gln Ala Met Gly Tyr Glu Val Asp Thr Ser Ser
 165 170 175
 Ala Ile Tyr Lys Gln Tyr Arg Leu Gln Lys Val Thr Glu Lys Tyr Pro
 180 185 190
 Glu Leu Gln Asn Leu Pro Gln Glu Leu Phe Ala Val Asp Pro Thr Thr
 195 200 205
 Val Ser Gln Gly Leu Lys Asp Glu Val Leu Tyr Lys Cys Arg Lys Cys
 210 215 220
 Arg Arg Ser Leu Phe Arg Ser Ser Ser Ile Leu Asp His Arg Glu Gly
 225 230 235 240
 Ser Gly Pro Ile Ala Phe Ala His Lys Arg Met Thr Pro Ser Ser Met
 245 250 255
 Leu Thr Thr Gly Arg Gln Ala Gln Cys Thr Ser Tyr Phe Ile Glu Pro
 260 265 270
 Val Gln Trp Met Glu Ser Ala Leu Leu Gly Val Met Asp Gly Gln Val
 275 280 285
 Arg Thr His Phe Ile Phe Tyr Asn Phe Ile Leu
 290 295

<210> 118
 <211> 1300
 <212> DNA
 <213> Homo sapiens

<400> 118
 cgggctggcc catggctgag acctctctcc cagagctggg gggagaggac aaagccacgc 60
 cttgccccag catcctggag ctggaggagc tctgcgggc agggaagtct tcttgacgcc 120

```

gtgtggacga agtttggccc aaccttttca taggagatgc agctgggtcct tactccctgc 180
catggggctc tgccactttg ccaccctggc actgatoctg ctgggtgctgc tggaggctct 240
ggcccaggcg gacacacaga agatgggtga agcccagcgt ggggtcggcc ctagagcctg 300
ctactccatc tggctcctcc tggcgctac accccctctc agccactgtc ttcagtctcc 360
acagaaacag catcaagtgt gcggagacag gcgggtgaaa gccagcagca cgaactgccc 420
gtcagagaag tgcacagcct gggccagata ctcccacagg atggactcac tgcagaagca 480
ggacctccgg agggccgaga tccatggggc agtccaggca tctccctacc agccgcccac 540
attggcttcg ctgcagcgt tgcgtgggt ccgtcaggct gccacactga accatatcga 600
tgaggctctg cccagcctct tccctgggaga tgcgtacgca gcccgggaca agagcaagct 660
gatccagctg ggaatcaccc acgttgtgaa tgcctgtgca ggcaagttcc aggtggacac 720
aggtgccaaa ttctaccgtg gaatgtccct ggagtactat ggcacgagg cggacgacaa 780
ccccctcttc gacctcagtg tctactttct gcctgttgct cgatacatcc gagctgccct 840
cagtgttccc caaggccgcg tgctggtaca ctgtgccatg ggggtaagcc gctctgccac 900
acttgtcctg gccttctca tgatctgtga gaacatgacg ctggtagagg ccatccagac 960
ggtgcaggcc caccgcaata tctgcctaa ctcaggcttc ctccggcagc tccaggttct 1020
ggacaaccga ctggggcggg agacggggcg gttctgatct ggcaggcagc caggatccct 1080
gaccttggc ccaacccac cagcctggcc ctgggaacag caggctctgc tgtttctagt 1140
gaccttgaga tgtaaacagc aagtgggggc tgaggcagag gcagggatag ctgggtggtg 1200
acctcttagc ggggtgattt ccctgaccca attcagagat tctttatgca aaagtgagtt 1260
cagtccatct ctataataaa atattcatcg tcataaagaa 1300

```

<210> 119

<211> 291

<212> PRT

<213> Homo sapiens

<400> 119

```

Met Gly Leu Cys His Phe Ala Thr Leu Ala Leu Ile Leu Leu Val Leu
 1           5           10           15
Leu Glu Ala Leu Ala Gln Ala Asp Thr Gln Lys Met Val Glu Ala Gln
      20           25           30
Arg Gly Val Gly Pro Arg Ala Cys Tyr Ser Ile Trp Leu Leu Leu Ala
      35           40           45
Pro Thr Pro Pro Leu Ser His Cys Leu Gln Ser Pro Gln Lys Gln His
      50           55           60
Gln Val Cys Gly Asp Arg Arg Leu Lys Ala Ser Ser Thr Asn Cys Pro
      65           70           75           80
Ser Glu Lys Cys Thr Ala Trp Ala Arg Tyr Ser His Arg Met Asp Ser
      85           90           95
Leu Gln Lys Gln Asp Leu Arg Arg Pro Glu Ile His Gly Ala Val Gln
      100          105          110
Ala Ser Pro Tyr Gln Pro Pro Thr Leu Ala Ser Leu Gln Arg Leu Leu
      115          120          125
Trp Val Arg Gln Ala Ala Thr Leu Asn His Ile Asp Glu Val Trp Pro
      130          135          140
Ser Leu Phe Leu Gly Asp Ala Tyr Ala Ala Arg Asp Lys Ser Lys Leu
      145          150          155          160
Ile Gln Leu Gly Ile Thr His Val Val Asn Ala Ala Ala Gly Lys Phe
      165          170          175
Gln Val Asp Thr Gly Ala Lys Phe Tyr Arg Gly Met Ser Leu Glu Tyr
      180          185          190
Tyr Gly Ile Glu Ala Asp Asp Asn Pro Phe Phe Asp Leu Ser Val Tyr
      195          200          205
Phe Leu Pro Val Ala Arg Tyr Ile Arg Ala Ala Leu Ser Val Pro Gln
      210          215          220
Gly Arg Val Leu Val His Cys Ala Met Gly Val Ser Arg Ser Ala Thr
      225          230          235          240
Leu Val Leu Ala Phe Leu Met Ile Cys Glu Asn Met Thr Leu Val Glu

```


245 250 255
 Ala Ile Gln Thr Val Gln Ala His Arg Asn Ile Cys Pro Asn Ser Gly
 260 265 270
 Phe Leu Arg Gln Leu Gln Val Leu Asp Asn Arg Leu Gly Arg Glu Thr
 275 280 285
 Gly Arg Phe
 290

<210> 120
 <211> 240
 <212> PRT
 <213> Homo sapiens

<400> 120
 Met Gly Leu Cys His Phe Ala Thr Leu Ala Leu Ile Leu Leu Val Leu
 1 5 10 15
 Leu Glu Ala Leu Ala Gln Ala Asp Thr Gln Lys Met Val Glu Ala Gln
 20 25 30
 Arg Gly Val Gly Pro Arg Ala Cys Tyr Ser Ile Trp Leu Leu Ala
 35 40 45
 Pro Thr Pro Pro Leu Ser His Cys Leu Gln Ser Pro Gln Lys Gln His
 50 55 60
 Gln Val Cys Gly Asp Arg Arg Leu Lys Ala Ser Ser Thr Asn Cys Pro
 65 70 75 80
 Ser Glu Lys Cys Thr Ala Trp Ala Arg Tyr Ser His Arg Met Asp Ser
 85 90 95
 Leu Gln Lys Gln Asp Leu Arg Arg Pro Glu Ile His Gly Ala Val Gln
 100 105 110
 Ala Ser Pro Tyr Gln Pro Pro Thr Leu Ala Ser Leu Gln Arg Leu Leu
 115 120 125
 Trp Val Arg Gln Ala Ala Thr Leu Asn His Ile Asp Glu Val Trp Pro
 130 135 140
 Ser Leu Phe Leu Gly Asp Ala Tyr Ala Ala Arg Asp Lys Ser Lys Leu
 145 150 155 160
 Ile Gln Leu Gly Ile Thr His Val Val Asn Ala Ala Ala Gly Arg Val
 165 170 175
 Leu Val His Cys Ala Met Gly Val Ser Arg Ser Ala Thr Leu Val Leu
 180 185 190
 Ala Phe Leu Met Ile Cys Glu Asn Met Thr Leu Val Glu Ala Ile Gln
 195 200 205
 Thr Val Gln Ala His Arg Asn Ile Cys Pro Asn Ser Gly Phe Leu Arg
 210 215 220
 Gln Leu Gln Val Leu Asp Asn Arg Leu Gly Arg Glu Thr Gly Arg Phe
 225 230 235 240

<210> 121
 <211> 935
 <212> DNA
 <213> Homo sapiens

<400> 121
 attgtgacgc ccagatggga gtggtgagag gagacagaaa gaggggtggtg gccgatagct 60
 ggtcctcttt ctccaacacc tagcctgaga cttggcggcg cggtgctat cctgaactag 120
 cttggtaagt gttgtgtccc gaaccagcgt agagagacct cggaccagcc gccttgatga 180
 cagcatccgc gtctccttt tcatcatctc aggggtgtcca gcagccctcc atctacagct 240
 tctcccaaat aaccagaagc ttgtttctca gcaatggtgt ggccgccaac gacaaactcc 300

```

ttctgtccag caatcgcatc accgccattg tcaatgcctc ggtggaagtg gtcaacgtat 360
tcttcgaggg cattcagtac ataaagggtgc ctgttaccga tgctcgtgac tcgctgtctc 420
acgacttttt tgacccattt gctgatctta tccacaccat cgatatgagg cagggccgta 480
cgctgctgca ctgcatggct ggagtgagec gtccgcctc actgtgcctt gcgtacctca 540
tgaaatatca ctccatgtcg ctgctggacg cccatacatg gaccaagtgc cgccgcccc 600
tcatccggcc caacaacggc ttttggaac agctcatcaa ttacgaattc aagctgttta 660
ataacaacac cgtgcgcgatg atcaactcgc cggtaggtaa catccctgac atctatgaga 720
aggacctacg tatgatgata tcaatgtaag ccacccggc cagccctga catctgccat 780
cgatcttgca ccaagactga acttgaacac tgacattttg ttagtaaaga aaaccggatg 840
gtgccttggt aaagggcaag aaaaaagga ggggggttga gttttgaac tagtaagcct 900
taccttaata gaattaaaaa aaaaaaaaaa aaaaa 935

```

<210> 122

<211> 190

<212> PRT

<213> Homo sapiens

<400> 122

```

Met Thr Ala Ser Ala Ser Ser Phe Ser Ser Ser Gln Gly Val Gln Gln
 1           5           10           15
Pro Ser Ile Tyr Ser Phe Ser Gln Ile Thr Arg Ser Leu Phe Leu Ser
      20           25           30
Asn Gly Val Ala Ala Asn Asp Lys Leu Leu Leu Ser Ser Asn Arg Ile
      35           40           45
Thr Ala Ile Val Asn Ala Ser Val Glu Val Val Asn Val Phe Phe Glu
      50           55           60
Gly Ile Gln Tyr Ile Lys Val Pro Val Thr Asp Ala Arg Asp Ser Arg
      65           70           75           80
Leu Tyr Asp Phe Phe Asp Pro Ile Ala Asp Leu Ile His Thr Ile Asp
      85           90           95
Met Arg Gln Gly Arg Thr Leu Leu His Cys Met Ala Gly Val Ser Arg
      100          105          110
Ser Ala Ser Leu Cys Leu Ala Tyr Leu Met Lys Tyr His Ser Met Ser
      115          120          125
Leu Leu Asp Ala His Thr Trp Thr Lys Ser Arg Arg Pro Ile Ile Arg
      130          135          140
Pro Asn Asn Gly Phe Trp Glu Gln Leu Ile Asn Tyr Glu Phe Lys Leu
      145          150          155          160
Phe Asn Asn Asn Thr Val Arg Met Ile Asn Ser Pro Val Gly Asn Ile
      165          170          175
Pro Asp Ile Tyr Glu Lys Asp Leu Arg Met Met Ile Ser Met
      180          185          190

```

<210> 123

<211> 1491

<212> DNA

<213> Homo sapiens

<400> 123

```

cgacagcagc aggagcgtca tggccgtggc gctgtctgcg ccggcgatcc gcctttcgga 60
ctgaggccca gcgcagcgtc tgcaaagagc agctacctgg caactgaacc catcatcacc 120
acagccactc ctgcagctgc cacggtttct gccacctcta agatgtgccc tggttaactgg 180
ctttgggctt ctatgacttt tatggcccgc ttctcccgga gtagtcaag gtctcctgtt 240
cgaactcgag ggaccctgga ggagatgcca accgttcaac atcctttcct caatgtcttc 300
gagttggagc ggctcctcta cacaggcaag acagcctgta accatgccga cgaggtctgg 360
ccaggcctct atctcggaga ccaggacatg gctaacaacc gccgggagct tcgccgcctg 420
ggcatcacgc acgtcctcaa tgctcacac agccggtggc gaggcacgcc cgaggcctat 480

```

```

gaggggctgg gcatacgccta cctgggtgtt gagggcccacg actcgccagc ctttgacatg 540
agcatccact tccagacggc tgccgacttc atccaccggg cgctgagcca gccaggaggg 600
aagatcctgg tgcatgtgtc tgtgggctgt agccgatccg ccaccctggg actggcatac 660
ctcatgctgt accaccacct taccctcgtg gagggccatca agaaagtcaa agaccaccga 720
ggcatcatcc ccaaccgggg ctccctgagg cagctcctgg ccctggaccg caggctgcgg 780
cagggctctgg aagcatgagg ggaggggggag agaggtcagg ccaggcccgt gggtaggtcc 840
ctggctccca gctggagata ggaggcccag gtggcaggta gcaggaggcc cagatcaccc 900
atcctccctt ggggtcagga gagggccgagc cccaggccac tgtcactctt tgtggggaggg 960
gacggggagt gaggttgggc agtgtggtgg atgggcaccc aggaagggtt gaccaggga 1020
ggaggcagct aggtgtaga tggaagatgg tctgtggatt cgaacaccgc tgggatctgg 1080
ccagggtgct ccctgggatt cacagtccct tccctctttt gtgccaagt gtttccctct 1140
ctccctcacc aaaacaaaag ggccatctct gccctgcact tgtgcagaaa gtcagggata 1200
cggcaagcat gaatgcaatg gtgtagagtt gtgtgaaacc cctagcatag agacagacag 1260
cgaagagatg gtgtgaaaag cttgcagaac cagacagaga accccacaga ctttccactc 1320
caagcacagg aggaggtagc tagcgtgtga ggggtggcac tagggccacg gctgctgctt 1380
gggcaaaaaa catacagagg tgcattgctg gcagtcttga aattgtcact cgcttactgg 1440
atccaagcgt ctcgaggata aataaagatc atgaaaaaca aaaaaaaaaa a 1491

```

<210> 124
 <211> 211
 <212> PRT
 <213> Homo sapiens

<400> 124

Met	Cys	Pro	Gly	Asn	Trp	Leu	Trp	Ala	Ser	Met	Thr	Phe	Met	Ala	Arg
1				5					10					15	
Phe	Ser	Arg	Ser	Ser	Ser	Arg	Ser	Pro	Val	Arg	Thr	Arg	Gly	Thr	Leu
			20					25					30		
Glu	Glu	Met	Pro	Thr	Val	Gln	His	Pro	Phe	Leu	Asn	Val	Phe	Glu	Leu
		35				40					45				
Glu	Arg	Leu	Leu	Tyr	Thr	Gly	Lys	Thr	Ala	Cys	Asn	His	Ala	Asp	Glu
	50					55					60				
Val	Trp	Pro	Gly	Leu	Tyr	Leu	Gly	Asp	Gln	Asp	Met	Ala	Asn	Asn	Arg
65					70					75				80	
Arg	Glu	Leu	Arg	Arg	Leu	Gly	Ile	Thr	His	Val	Leu	Asn	Ala	Ser	His
			85						90					95	
Ser	Arg	Trp	Arg	Gly	Thr	Pro	Glu	Ala	Tyr	Glu	Gly	Leu	Gly	Ile	Arg
			100					105					110		
Tyr	Leu	Gly	Val	Glu	Ala	His	Asp	Ser	Pro	Ala	Phe	Asp	Met	Ser	Ile
		115					120					125			
His	Phe	Gln	Thr	Ala	Ala	Asp	Phe	Ile	His	Arg	Ala	Leu	Ser	Gln	Pro
		130				135					140				
Gly	Gly	Lys	Ile	Leu	Val	His	Cys	Ala	Val	Gly	Val	Ser	Arg	Ser	Ala
145				150						155				160	
Thr	Leu	Val	Leu	Ala	Tyr	Leu	Met	Leu	Tyr	His	His	Leu	Thr	Leu	Val
			165						170					175	
Glu	Ala	Ile	Lys	Lys	Val	Lys	Asp	His	Arg	Gly	Ile	Ile	Pro	Asn	Arg
		180						185					190		
Gly	Phe	Leu	Arg	Gln	Leu	Leu	Ala	Leu	Asp	Arg	Arg	Leu	Arg	Gln	Gly
		195				200						205			
Leu	Glu	Ala													
		210													

<210> 125
 <211> 1830
 <212> DNA
 <213> Homo sapiens

<400> 125

```

gaagaggagc gccagatggt ggaggaatac acttatttat gaaactgtct tgagttcttc 60
ttgaattgcc agttttcagc ctctctcatgc ctccgtctcc tttagacgac agggtagtag 120
tggcactatc tagggccgtc cgacctcagg atctcaacct ttgttttagac tctagttacc 180
ttggctctgc caaccaggc agtaacagcc accctcctgt catcgccacc accgttgtgt 240
ccctcaaggc tgcgaatctg acgtatatgc cctcatccag cggctctgcc cgctcgctga 300
attgtggatg cagcagtgcc agctgctgca ctgtggcaac ctacgacaag gacaatcagg 360
cccaaaccce agccattgcc gctggcacca ccaccactgc catcggaacc tctaccacct 420
gccctgctaa ccagatggtc aacaataatg aaaatacagg ctctctaagt ccatcaagtg 480
gggtgggcag ccctgtgtca gggaccccca agcagctagc cagcatcaaa ataatctacc 540
ccaatgactt ggcaaagaag atgaccaa atgcagcaagag tcacctgccg agtcagggcc 600
ctgtcatcat tgactgcagg cccttcatgg agtacaacaa gagtcacatc caaggagctg 660
tccacattaa ctgtgccgat aagatcagcc ggcggagact gcagcagggc aagatcactg 720
tcttagactt gatttctgt aggggaaggca aggactcttt caagaggatc ttttccaaag 780
aaattatagt ttatgatgag aataccaatg aaccaagccg agtgatgccc tcccagccac 840
ttcacatagt cctcgagtc ctgaagagag aaggcaaaga acctctggtg ttgaaagggtg 900
gacttagtag ttttaagcag aaccatgaaa acctctgtga caactccctc cagctccaag 960
agtgcgggga ggtggggggc ggcgcacccg cggcctcgag cttgctacct cagcccatcc 1020
ccaccacccc tgacatcgag aacgctgagc tcaccccat cttgcccttc ctgttccctg 1080
gcaatgagca ggatgctcag gacctggaca ccatgcagcg gctgaacatc ggctacgtca 1140
tcaacgtcac cactcatctt cccctctacc actatgagaa aggcctgttc aactacaagc 1200
ggctgccagc cactgacagc aacaagcaga acctgcggca gtactttgaa gaggcttttg 1260
agttcattga ggaagctcac cagtgtggga aggggcttct catccactgc caggctgggg 1320
tgtcccgctc cgccaccatc gtcacgctt acttgatgaa gcacactcgg atgaccatga 1380
ctgatgctta taaatttgtc aaaggcaaac gaccaattat ctcccaaac cttaacttca 1440
tggggcagtt gctagagttc gaggaagacc taaacaacgg tgtgacaccg agaatcctta 1500
caccaaagct gatgggcgtg gagacggttg tgtgacaatg gtctggatgg aaaggattgc 1560
tgctctccat taggagacaa tgaggaagga ggatggattc tgggtttttt tctttctttt 1620
tttttttgta gttgggagta agtttgtgaa tggaaacaaa cttgttttaa cactttattt 1680
ttaacaagtg taagaagact ataacttttg atgccattga gattcacctc ccacaaactg 1740
acaaattaag gaggttaaag aagtaatttt ttaagccaa caataaaaaat ataatgcca 1800
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa

```

1830

<210> 126

<211> 482

<212> PRT

<213> Homo sapiens

<400> 126

```

Met Pro Pro Ser Pro Leu Asp Asp Arg Val Val Val Ala Leu Ser Arg
 1           5           10           15
Pro Val Arg Pro Gln Asp Leu Asn Leu Cys Leu Asp Ser Ser Tyr Leu
 20           25           30
Gly Ser Ala Asn Pro Gly Ser Asn Ser His Pro Pro Val Ile Ala Thr
 35           40           45
Thr Val Val Ser Leu Lys Ala Ala Asn Leu Thr Tyr Met Pro Ser Ser
 50           55           60
Ser Gly Ser Ala Arg Ser Leu Asn Cys Gly Cys Ser Ser Ala Ser Cys
 65           70           75           80
Cys Thr Val Ala Thr Tyr Asp Lys Asp Asn Gln Ala Gln Thr Gln Ala
 85           90           95
Ile Ala Ala Gly Thr Thr Thr Thr Ala Ile Gly Thr Ser Thr Thr Cys
100           105           110
Pro Ala Asn Gln Met Val Asn Asn Asn Glu Asn Thr Gly Ser Leu Ser
115           120           125
Pro Ser Ser Gly Val Gly Ser Pro Val Ser Gly Thr Pro Lys Gln Leu
130           135           140

```

Ala Ser Ile Lys Ile Ile Tyr Pro Asn Asp Leu Ala Lys Lys Met Thr
 145 150 155 160
 Lys Cys Ser Lys Ser His Leu Pro Ser Gln Gly Pro Val Ile Ile Asp
 165 170 175
 Cys Arg Pro Phe Met Glu Tyr Asn Lys Ser His Ile Gln Gly Ala Val
 180 185 190
 His Ile Asn Cys Ala Asp Lys Ile Ser Arg Arg Arg Leu Gln Gln Gly
 195 200 205
 Lys Ile Thr Val Leu Asp Leu Ile Ser Cys Arg Glu Gly Lys Asp Ser
 210 215 220
 Phe Lys Arg Ile Phe Ser Lys Glu Ile Ile Val Tyr Asp Glu Asn Thr
 225 230 235 240
 Asn Glu Pro Ser Arg Val Met Pro Ser Gln Pro Leu His Ile Val Leu
 245 250 255
 Glu Ser Leu Lys Arg Glu Gly Lys Glu Pro Leu Val Leu Lys Gly Gly
 260 265 270
 Leu Ser Ser Phe Lys Gln Asn His Glu Asn Leu Cys Asp Asn Ser Leu
 275 280 285
 Gln Leu Gln Glu Cys Arg Glu Val Gly Gly Gly Ala Ser Ala Ala Ser
 290 295 300
 Ser Leu Leu Pro Gln Pro Ile Pro Thr Thr Pro Asp Ile Glu Asn Ala
 305 310 315 320
 Glu Leu Thr Pro Ile Leu Pro Phe Leu Phe Leu Gly Asn Glu Gln Asp
 325 330 335
 Ala Gln Asp Leu Asp Thr Met Gln Arg Leu Asn Ile Gly Tyr Val Ile
 340 345 350
 Asn Val Thr Thr His Leu Pro Leu Tyr His Tyr Glu Lys Gly Leu Phe
 355 360 365
 Asn Tyr Lys Arg Leu Pro Ala Thr Asp Ser Asn Lys Gln Asn Leu Arg
 370 375 380
 Gln Tyr Phe Glu Glu Ala Phe Glu Phe Ile Glu Glu Ala His Gln Cys
 385 390 395 400
 Gly Lys Gly Leu Leu Ile His Cys Gln Ala Gly Val Ser Arg Ser Ala
 405 410 415
 Thr Ile Val Ile Ala Tyr Leu Met Lys His Thr Arg Met Thr Met Thr
 420 425 430
 Asp Ala Tyr Lys Phe Val Lys Gly Lys Arg Pro Ile Ile Ser Pro Asn
 435 440 445
 Leu Asn Phe Met Gly Gln Leu Leu Glu Phe Glu Glu Asp Leu Asn Asn
 450 455 460
 Gly Val Thr Pro Arg Ile Leu Thr Pro Lys Leu Met Gly Val Glu Thr
 465 470 475 480
 Val Val

<210> 127

<211> 707

<212> DNA

<213> Homo sapiens

<400> 127

tgaccgctg tctgtgccc tttcccagcg atgggctgc agcccccaa cttctcctgg 60
 gtgcttccgg gccggtggc gggactggcg ctgcgcggc tccccgcca ctaccagttc 120
 ctgttggaac tgggctgctg gcacctggtg tccctgacgg agcgcggggc ccctcacagc 180
 gacagctgcc ccggcctcac cctgcaccgc ctgcgcattc ccgacttctg cccgccggcc 240
 cccgaccaga tcgaccgctt cgtgcagatc gtggacgagg ccaacgcacg gggagaggct 300
 gtgggagtgc actgtgctct gggctttggc cgcactggca ccattgctggc ctgttacctg 360

```

gtgaaggagc ggggcttggc tgcaggagat gccattgctg aaatccgacg actacgaccc 420
ggctccatcg agacctatga gcaggagaaa gcagtcttcc agttctacca gcgaacgaaa 480
taaggggctt tagtaccctt ctaccaggcc ctactcccc ttcccatgtg tgtcgatggg 540
gccagagatg aagggaagtg gactaaagta ttaaaccctc tagctcccat tggctgaaga 600
cactgaagta gccaccctt gcaggcaggt cctgattgaa ggggaggctt gtactgcttt 660
gttgaataaa tgagttttac gaaccaaaaa aaaaaaaaaa aaaaaaa 707

```

<210> 128

<211> 150

<212> PRT

<213> Homo sapiens

<400> 128

```

Met Gly Val Gln Pro Pro Asn Phe Ser Trp Val Leu Pro Gly Arg Leu
 1           5           10           15
Ala Gly Leu Ala Leu Pro Arg Leu Pro Ala His Tyr Gln Phe Leu Leu
 20           25           30
Asp Leu Gly Val Arg His Leu Val Ser Leu Thr Glu Arg Gly Pro Pro
 35           40           45
His Ser Asp Ser Cys Pro Gly Leu Thr Leu His Arg Leu Arg Ile Pro
 50           55           60
Asp Phe Cys Pro Pro Ala Pro Asp Gln Ile Asp Arg Phe Val Gln Ile
 65           70           75           80
Val Asp Glu Ala Asn Ala Arg Gly Glu Ala Val Gly Val His Cys Ala
 85           90           95
Leu Gly Phe Gly Arg Thr Gly Thr Met Leu Ala Cys Tyr Leu Val Lys
100          105          110
Glu Arg Gly Leu Ala Ala Gly Asp Ala Ile Ala Glu Ile Arg Arg Leu
115          120          125
Arg Pro Gly Ser Ile Glu Thr Tyr Glu Gln Glu Lys Ala Val Phe Gln
130          135          140
Phe Tyr Gln Arg Thr Lys
145          150

```

<210> 129

<211> 1949

<212> DNA

<213> Homo sapiens

<400> 129

```

aagcagtggg aacaacgcag agtacgcggg cgaggagaa atcttgctgg gaggggactt 60
ttccagtaag gaaagtaaaa gctgcacccat tgggatgggt ctccgactgt ggagcgacac 120
gaaaatccac cttgatggag atgggtgggt cagcgtgagc acagcaggaa ggatgcacat 180
atttaagcct gtgtctgtcc aggccatgtg gtctgccctg cagggtgcttc acaaggcctg 240
cgaagtggcc cggaggcaca actacttccc cgggggtgta gctctcatct gggctaccta 300
ctatgagagc tgcatacagc ccgagcagag ctgcatcaac gagggtgaac ccatgcagga 360
cctggagtct acgcggcccg actccccgcg gctatttgtg gacaagccca ctgaagggga 420
aaggaccgag cgcctcatca aagccaagct ccgaagcacc atgatgagcc aggatctaga 480
aaatgtgact tccaaagaga ttcgtaatga attagagaaa cagatgaatt gtaacttgaa 540
ggaactcaag gaatttatag acaatgagat gctacttacc ttgggacaga tggacaagcc 600
ctcccttacc ttcgatcacc tttatctcgg ctctgaattg aatgcatcca atctggagga 660
actgcagggc tcaggggttg attacatttt aaatggtacc agagaaatcg ataatttttt 720
tcttggttta tttgcatatc ataacatccg agtctacgat gaagagacca cagacctcct 780
cgccactgg aatgaagcgt atcattttat aaacaaagcg aagaggaacc attccaagt 840
cctggtgcat tgcaaaatgg gcgtgagtcg ctgggcctcc acagtcatag cctatgcaat 900
gaaggaattc ggctggcctc tggaaaaagc atataactat gtaaagcaga agcgcagcat 960
cacgcgcccc aacgcgggct ttatgaggca gctgtctgag tatgaaggca tcttggatgc 1020

```

```

aagcaaacag cggcacaaca agctgtggcg tcagcagaca gacagcagcc tccagcagcc 1080
tgtggatgac cctgcaggac ctggcgactt cttgccagag accccagatg gcaccccgga 1140
aagccagctg cccttcttgg atgatgcgc ccagcccgcc ttagggcccc ccctccctg 1200
ctgtttccgg cgactctcag accccttctt gccttccctt gaggatgaag ccggcagctt 1260
ggtccacctg gaggatccgg agagggaggc tctgttggag gaagctgctc cacctgcaga 1320
ggtgcacagg cgggccagac agccccagca aggttccgga ctctgtgaga aggatgtgaa 1380
gaagaaacta gagtttggga gtcccaaagg tcggagcggc tccttgctgc aggtggagga 1440
gacggaaagg gaggagggcc tgggagcagg gaggtggggg cagcttccaa cccagctcga 1500
tcaaacctg ctcaactcgg agaacctaaa caacaacagc aagaggagct gtcccaacgg 1560
catggaggtg ggcagagccc ggctgcagg gtggcacacc ccatcccttc catccactc 1620
taattggcct acctcagcct ctgtagtagg gactacaggc acccgccacc acaccagct 1680
gatttttttc tattgtctcc tctgggcccc cagctcccat ctccagggac ctgagggttc 1740
tttcacaggg tgattctgct ggtgggtacg tagtgcatac cttatatagc aaattgagaa 1800
tctgttggga ataacacata tctctgcaca ccattctcac cccatgtacc ttattcatat 1860
cctgggcagg gcttccaact caatttcttt ttgtgtatgt aaaattaaaa catataattt 1920
atcagccaaa aaaaaaaaaa aaaaaaaaaa

```

<210> 130

<211> 552

<212> PRT

<213> Homo sapiens

<400> 130

```

Met Val Leu Arg Leu Trp Ser Asp Thr Lys Ile His Leu Asp Gly Asp
 1           5           10           15
Gly Gly Phe Ser Val Ser Thr Ala Gly Arg Met His Ile Phe Lys Pro
 20           25           30
Val Ser Val Gln Ala Met Trp Ser Ala Leu Gln Val Leu His Lys Ala
 35           40           45
Cys Glu Val Ala Arg Arg His Asn Tyr Phe Pro Gly Gly Val Ala Leu
 50           55           60
Ile Trp Ala Thr Tyr Tyr Glu Ser Cys Ile Ser Ser Glu Gln Ser Cys
 65           70           75           80
Ile Asn Glu Trp Asn Ala Met Gln Asp Leu Glu Ser Thr Arg Pro Asp
 85           90           95
Ser Pro Ala Leu Phe Val Asp Lys Pro Thr Glu Gly Glu Arg Thr Glu
100          105          110
Arg Leu Ile Lys Ala Lys Leu Arg Ser Ile Met Met Ser Gln Asp Leu
115          120          125
Glu Asn Val Thr Ser Lys Glu Ile Arg Asn Glu Leu Glu Lys Gln Met
130          135          140
Asn Cys Asn Leu Lys Glu Leu Lys Glu Phe Ile Asp Asn Glu Met Leu
145          150          155          160
Leu Ile Leu Gly Gln Met Asp Lys Pro Ser Leu Ile Phe Asp His Leu
165          170          175
Tyr Leu Gly Ser Glu Trp Asn Ala Ser Asn Leu Glu Glu Leu Gln Gly
180          185          190
Ser Gly Val Asp Tyr Ile Leu Asn Val Thr Arg Glu Ile Asp Asn Phe
195          200          205
Phe Pro Gly Leu Phe Ala Tyr His Asn Ile Arg Val Tyr Asp Glu Glu
210          215          220
Thr Thr Asp Leu Leu Ala His Trp Asn Glu Ala Tyr His Phe Ile Asn
225          230          235          240
Lys Ala Lys Arg Asn His Ser Lys Cys Leu Val His Cys Lys Met Gly
245          250          255
Val Ser Arg Ser Ala Ser Thr Val Ile Ala Tyr Ala Met Lys Glu Phe
260          265          270
Gly Trp Pro Leu Glu Lys Ala Tyr Asn Tyr Val Lys Gln Lys Arg Ser

```

[illegible]

```
<210> 131
<211> 1711
<212> DNA
<213> Homo sapiens
```

<400> 131						
cctgggaaga	agttatctat	ctctcgagtg	acattcaaga	tataccgtac	ccctcggttc	60
tgtaatcct	ctaagttgga	ggcattccat	tctgagccgg	ccccatgacc	ctgagcacgt	120
tggcccgcaa	gaggaaggcg	cccctcgctt	gcacctgcag	cctcggtggc	cccgacatga	180
ttccttactt	ctccgccaac	gcggtcatct	cgcagaacgc	catcaaccag	ctcatcagcg	240
agagctttct	aactgtcaaa	ggtgctgccc	ttttctacc	acggggaaat	ggctcatcca	300
caccaagaat	cagccacaga	cggaacaagc	atgcaggcga	tctccaacag	catctccaag	360
caatgttcat	tttactccgc	ccagaagaca	acatcaggct	ggctgtaaga	ctggaaagta	420
cttaccagaa	tcgaacacgc	tatatggtag	tggtttcaac	taatggtaga	caagacactg	480
aagaaagcat	cgtcctagga	atggatttct	cctctaataa	cagtagcact	tgtaccatgg	540
gcttagtttt	gcctctctgg	agcgacacgc	taattcattt	ggatggtgat	ggtgggttca	600
gtgtatcgac	ggataacaga	gttcacatat	tcaaacctgt	atctgtgcag	gcaatgtggt	660
ctgactaca	gagctttacac	aaggcttggt	aagtcgccag	agcgcataac	tactaccag	720
gcagcttatt	tctcacttgg	gtgagttatt	atgagagcca	tatcaactca	gatcaactct	780
cagtcaatga	atggaatgca	atgcaagatg	tacagtccca	cgggcccgc	tctccagctc	840
tcttcaccga	catacctact	gaacgtgaac	gaacagaaaag	gctaattaaa	accaaattaa	900


```

gggagatcat gatgcagaag gatttggaga atattacatc caaagagata agaacagagt 960
tggaatgca aatggtgtgc aacttgcggg aattcaagga atttatagac aatgaaatga 1020
tagtgatcct tgggtcaaag gatagcccta cacagatatt tgagcatgtg ttcctgggct 1080
cagaatggaa tgcctccaac ttagaggact tacagaaccg aggggtacgg tataatcttga 1140
atgtcactcg agagatagat aacttcttcc caggagtctt tgagtatcat aacattcggg 1200
tatatgatga agaggcaacg gatctcctgg cgtactggaa tgacacttac aaattcatct 1260
ctaaagcaaa gaaacatgga tctaaatgcc ttgtgactg caaaatgggg gtgagtcgct 1320
cagcctccac cgtgattgcc tatgcaatga aggaatatgg ctggaatctg gaccgagcct 1380
atgactatgt gaaagaaaga cgaacggtaa ccaagcccaa cccaagcttc atgagacaac 1440
tggaagagta tcaggggatc ttgctggcaa gcttcctagg cttgattcat ggagggaggg 1500
acaagccctg gggagagaaa agcacagaat ttgagtcagt agatctgggt tccattcctg 1560
gttcaccctc ttgctgcaac cctgagaagt tacttcacat ttctcctcct tacctgaccc 1620
catctataaa atgaaaatca agagatccat ctcacagggt tattgtgaat aaaaatgtgt 1680
ttgaatgttt ataaaaaaaa aaaaaaaaaa a 1711

```

<210> 132

<211> 509

<212> PRT

<213> Homo sapiens

<400> 132

```

Met Thr Leu Ser Thr Leu Ala Arg Lys Arg Lys Ala Pro Leu Ala Cys
1          5          10          15
Thr Cys Ser Leu Gly Gly Pro Asp Met Ile Pro Tyr Phe Ser Ala Asn
          20          25          30
Ala Val Ile Ser Gln Asn Ala Ile Asn Gln Leu Ile Ser Glu Ser Phe
          35          40          45
Leu Thr Val Lys Gly Ala Ala Leu Phe Leu Pro Arg Gly Asn Gly Ser
          50          55          60
Ser Thr Pro Arg Ile Ser His Arg Arg Asn Lys His Ala Gly Asp Leu
65          70          75          80
Gln Gln His Leu Gln Ala Met Phe Ile Leu Leu Arg Pro Glu Asp Asn
          85          90          95
Ile Arg Leu Ala Val Arg Leu Glu Ser Thr Tyr Gln Asn Arg Thr Arg
          100          105          110
Tyr Met Val Val Val Ser Thr Asn Gly Arg Gln Asp Thr Glu Glu Ser
          115          120          125
Ile Val Leu Gly Met Asp Phe Ser Ser Asn Asp Ser Ser Thr Cys Thr
          130          135          140
Met Gly Leu Val Leu Pro Leu Trp Ser Asp Thr Leu Ile His Leu Asp
145          150          155          160
Gly Asp Gly Gly Phe Ser Val Ser Thr Asp Asn Arg Val His Ile Phe
          165          170          175
Lys Pro Val Ser Val Gln Ala Met Trp Ser Ala Leu Gln Ser Leu His
          180          185          190
Lys Ala Cys Glu Val Ala Arg Ala His Asn Tyr Tyr Pro Gly Ser Leu
          195          200          205
Phe Leu Thr Trp Val Ser Tyr Tyr Glu Ser His Ile Asn Ser Asp Gln
          210          215          220
Ser Ser Val Asn Glu Trp Asn Ala Met Gln Asp Val Gln Ser His Arg
225          230          235          240
Pro Asp Ser Pro Ala Leu Phe Thr Asp Ile Pro Thr Glu Arg Glu Arg
          245          250          255
Thr Glu Arg Leu Ile Lys Thr Lys Leu Arg Glu Ile Met Met Gln Lys
          260          265          270
Asp Leu Glu Asn Ile Thr Ser Lys Glu Ile Arg Thr Glu Leu Glu Met
          275          280          285
Gln Met Val Cys Asn Leu Arg Glu Phe Lys Glu Phe Ile Asp Asn Glu

```

290	295	300
Met Ile Val Ile Leu Gly Gln Met Asp Ser Pro Thr Gln Ile Phe Glu		
305	310	315
His Val Phe Leu Gly Ser Glu Trp Asn Ala Ser Asn Leu Glu Asp Leu		
	325	330
Gln Asn Arg Gly Val Arg Tyr Ile Leu Asn Val Thr Arg Glu Ile Asp		
	340	345
Asn Phe Phe Pro Gly Val Phe Glu Tyr His Asn Ile Arg Val Tyr Asp		
	355	360
Glu Glu Ala Thr Asp Leu Leu Ala Tyr Trp Asn Asp Thr Tyr Lys Phe		
	370	375
Ile Ser Lys Ala Lys Lys His Gly Ser Lys Cys Leu Val His Cys Lys		
385	390	395
Met Gly Val Ser Arg Ser Ala Ser Thr Val Ile Ala Tyr Ala Met Lys		
	405	410
Glu Tyr Gly Trp Asn Leu Asp Arg Ala Tyr Asp Tyr Val Lys Glu Arg		
	420	425
Arg Thr Val Thr Lys Pro Asn Pro Ser Phe Met Arg Gln Leu Glu Glu		
	435	440
Tyr Gln Gly Ile Leu Leu Ala Ser Phe Leu Gly Leu Ile His Gly Gly		
	450	455
Arg Asp Lys Pro Trp Gly Glu Lys Ser Thr Glu Phe Glu Ser Val Asp		
465	470	475
Leu Val Ser Ile Pro Gly Ser Pro Ser Cys Cys Asn Pro Glu Lys Leu		
	485	490
Leu His Ile Ser His Pro Tyr Leu Thr Pro Ser Ile Lys		
	500	505

<210> 133
 <211> 1165
 <212> DNA
 <213> Homo sapiens

<400> 133
 ggccagtgagg ggtgggctggg cgtgcgggctg ctacatgccc cacggaccag aacctcccca 60
 cgcgccaggg ccccggcaca ccagctgca gaaaggagag aaaatccctt ggctctaaaa 120
 tgacatctgg agaagtgaag acaagcctca agaatgccta ctcatctgcc aagaggctgt 180
 cgccgaagat ggaggaggaa ggggaggagg aggactactg cacccttgga gcctttgagc 240
 tggagcggct cttctggaag ggcagtcctc agtacacca cgtcaacgag gtctggccca 300
 agctctacat tggcgatgag ggcagggcgc tggaccgcta taggctgcag aaggcggggg 360
 tcacgcacgt gctgaacgcg gcccacggcc gctggaacgt ggacactggg cccgactact 420
 accgcgacat ggacatccag taccacggcg tggaggccga cgacctgccc accttcgacc 480
 tcagtgtctt cttctaccog gcggcagcct tcatcgacag agcgctaagc gacgaccaca 540
 gtaagatcct ggttcaactgc gtcattgggccc gcagccgggtc agccaccctg gtcctggcct 600
 acctgatgat ccacaaggac atgaccctgg tggacgccat ccagcaagtg gccaagaacc 660
 gctgcgtcct cccgaaccgg ggctttttga agcagctccg ggagctggac aagcagctgg 720
 tgcagcagag ggcagcggcc cagegccagg acggtgagga ggaggatggc agggagctgt 780
 agggccgact cacagggccca gcagaggcac ttggggacag aggggagagg cagaacatag 840
 ccctggccta ggactccaga gaagggatgg tgaaaccgaa gctcgactct tccaaaccat 900
 cttgttcaac ttccccatgt gtgctgggga caggaggagg ccagagctgc ccccgggcag 960
 agctgagcgc tcagcctctc agcaaaatgg gagggacggg ctccccggct ctgggtcaca 1020
 gaggagcatg ccacgctgca ccaagtctcc tgctttgggt ttgttttttt ggtgagaagg 1080
 aagagggaaa aagattttta aaatgtgtag gcagtatggt gtgattaaac gtttggcttt 1140
 gtccaaaaaa aaaaaaaaaa aaaaa 1165

<210> 134
 <211> 220

<212> PRT

<213> Homo sapiens

<400> 134

```

Met Thr Ser Gly Glu Val Lys Thr Ser Leu Lys Asn Ala Tyr Ser Ser
 1           5           10           15
Ala Lys Arg Leu Ser Pro Lys Met Glu Glu Glu Gly Glu Glu Asp
 20           25           30
Tyr Cys Thr Pro Gly Ala Phe Glu Leu Glu Arg Leu Phe Trp Lys Gly
 35           40           45
Ser Pro Gln Tyr Thr His Val Asn Glu Val Trp Pro Lys Leu Tyr Ile
 50           55           60
Gly Asp Glu Ala Thr Ala Leu Asp Arg Tyr Arg Leu Gln Lys Ala Gly
 65           70           75           80
Phe Thr His Val Leu Asn Ala Ala His Gly Arg Trp Asn Val Asp Thr
 85           90           95
Gly Pro Asp Tyr Tyr Arg Asp Met Asp Ile Gln Tyr His Gly Val Glu
100          105          110
Ala Asp Asp Leu Pro Thr Phe Asp Leu Ser Val Phe Phe Tyr Pro Ala
115          120          125
Ala Ala Phe Ile Asp Arg Ala Leu Ser Asp Asp His Ser Lys Ile Leu
130          135          140
Val His Cys Val Met Gly Arg Ser Arg Ser Ala Thr Leu Val Leu Ala
145          150          155          160
Tyr Leu Met Ile His Lys Asp Met Thr Leu Val Asp Ala Ile Gln Gln
165          170          175
Val Ala Lys Asn Arg Cys Val Leu Pro Asn Arg Gly Phe Leu Lys Gln
180          185          190
Leu Arg Glu Leu Asp Lys Gln Leu Val Gln Gln Arg Arg Arg Ser Gln
195          200          205
Arg Gln Asp Gly Glu Glu Glu Asp Gly Arg Glu Leu
210          215          220

```

<210> 135

<211> 1980

<212> DNA

<213> Homo sapiens

<400> 135

```

atggccctgg tcacagtgag ccgttcgccc ccgggcagcg ggcgcctccac gcccggtgggg 60
ccctgggacc aggcggtcca gcgaaggagt cgactccagc gaaggcagag ctttgcggtg 120
ctccgtgggg ctgtcctggg actgcaggat ggaggggaca atgatgatgc agcagaggcc 180
agttctgagc caacagagaa ggccccgagt gaggaggagc tccacgggga ccagacagac 240
ttcgggcaag gatcccagag tcccagaag caggaggagc agaggcagca cctgcacctc 300
atggtacagc tgctgaggcc gcaggatgac atccgcctgg cagcccagct ggaggcaccc 360
cggcctcccc ggctccgcta cctgctggta gtttctacac gagaaggaga aggtctgagc 420
caggatgaga cggtcctcct gggcgtggat ttccctgaca gcagctcccc cagctgcacc 480
ctgggcctgg tcttgcccct ctggagtgc acccaggtgt acttagatgg agacgggggc 540
ttcagcgtga cgtctggtgg gcaaagccgg atcttcaagc ccatctccat ccagaccatg 600
tgggccacac tccaggtatt gcaccaagca tgtgaggcag ctctaggcag cggccttgta 660
ccgggtggca gtgcctcac ctgggccagc cactaccagg agagactgaa ctccgaacag 720
agctgcctca atgagtggac ggctatggcc gacctggagt ctctgcggcc tcccagcgcc 780
gagcctggcg ggtcctcaga acaggagcag atggagcagg cgatccgtgc tgagctgtgg 840
aaagtgttgg atgtcagtga cctggagagt gtcacttcca aagagatccg ccaggctctg 900
gagctgcgcc tggggctccc cctccagcag taccgtgact tcatcgacaa ccagatgctg 960
ctgctggtgg cacagcggga ccgagcctcc cgcattctcc cccacctcta cctgggctca 1020
gagtggaaac cagcaaacct ggaggagctg cagaggaaca gggtcaccca catcttgaac 1080

```

```

atggccccggg agattgacaa cttctaccct gagcgcttca cctaccacaa tgtgcgcttc 1140
tgggatgagg agtcggccca gctgctgccg cactggaagg agacgcaccg cttcattgag 1200
gctgcaagag cacagggcac ccacgtgctg gtccactgca agatgggcgt cagccgctca 1260
gcggccacag tgctggccta tgccatgaag cagtacgaat gcagcctgga gcaggccctg 1320
cgccacgtgc aggagctccg gcccatcgcc cgcccccaacc ctggcttcct gcgccagctg 1380
cagatctacc agggcatcct gacggccagc cgccagagcc atgtctggga gcagaaagtg 1440
ggtgggggtct ccccagagga gaccccagcc cctgaagtct ctacaccatt cccacctctt 1500
ccgccagaac ctgaggggtg tggggaggag aaggttgtag gcatggaaga gagccaggca 1560
gccccgaaag aagagcctgg gccacggcca cgtataaacc tccgaggggt catgaggtcc 1620
atcagtcctt tggagccctc cttggagctg gagagcacct cagagaccag tgacatgcca 1680
gaggtcttct cttcccacga gtcttcacat gaagagcctc tgcagccctt cccacagctt 1740
gcaaggacca agggaggcca gcaggtggac agggggcctc agcctgccct gaagtcccgc 1800
cagtcagtgg ttaccctcca gggcagtgcc gtggtggcca accggacca ggccttccag 1860
gagcaggagc aggggcaggg gcaggggcag ggagagccct gcatttcctc tacgcccagg 1920
ttccggaagg tggtagaca ggccagcgtg catgacagtg gagaggaggg cgaggcctga 1980

```

<210> 136

<211> 659

<212> PRT

<213> Homo sapiens

<400> 136

```

Met Ala Leu Val Thr Val Ser Arg Ser Pro Pro Gly Ser Gly Ala Ser
1          5          10          15
Thr Pro Val Gly Pro Trp Asp Gln Ala Val Gln Arg Arg Ser Arg Leu
20         25         30
Gln Arg Arg Gln Ser Phe Ala Val Leu Arg Gly Ala Val Leu Gly Leu
35         40         45
Gln Asp Gly Gly Asp Asn Asp Ala Ala Glu Ala Ser Ser Glu Pro
50         55         60
Thr Glu Lys Ala Pro Ser Glu Glu Glu Leu His Gly Asp Gln Thr Asp
65         70         75         80
Phe Gly Gln Gly Ser Gln Ser Pro Gln Lys Gln Glu Glu Gln Arg Gln
85         90         95
His Leu His Leu Met Val Gln Leu Leu Arg Pro Gln Asp Asp Ile Arg
100        105        110
Leu Ala Ala Gln Leu Glu Ala Pro Arg Pro Pro Arg Leu Arg Tyr Leu
115        120        125
Leu Val Val Ser Thr Arg Glu Gly Glu Gly Leu Ser Gln Asp Glu Thr
130        135        140
Val Leu Leu Gly Val Asp Phe Pro Asp Ser Ser Ser Pro Ser Cys Thr
145        150        155        160
Leu Gly Leu Val Leu Pro Leu Trp Ser Asp Thr Gln Val Tyr Leu Asp
165        170        175
Gly Asp Gly Gly Phe Ser Val Thr Ser Gly Gly Gln Ser Arg Ile Phe
180        185        190
Lys Pro Ile Ser Ile Gln Thr Met Trp Ala Thr Leu Gln Val Leu His
195        200        205
Gln Ala Cys Glu Ala Ala Leu Gly Ser Gly Leu Val Pro Gly Gly Ser
210        215        220
Ala Leu Thr Trp Ala Ser His Tyr Gln Glu Arg Leu Asn Ser Glu Gln
225        230        235        240
Ser Cys Leu Asn Glu Trp Thr Ala Met Ala Asp Leu Glu Ser Leu Arg
245        250        255
Pro Pro Ser Ala Glu Pro Gly Gly Ser Ser Glu Gln Glu Gln Met Glu
260        265        270
Gln Ala Ile Arg Ala Glu Leu Trp Lys Val Leu Asp Val Ser Asp Leu

```

275	280	285
Glu Ser Val Thr Ser Lys	Glu Ile Arg Gln Ala Leu	Glu Leu Arg Leu
290	295	300
Gly Leu Pro Leu Gln Gln Tyr Arg Asp Phe Ile Asp Asn Gln Met Leu		
305	310	315
Leu Leu Val Ala Gln Arg Asp Arg Ala Ser Arg Ile Phe Pro His Leu		
325	330	335
Tyr Leu Gly Ser Glu Trp Asn Ala Ala Asn Leu Glu Glu Leu Gln Arg		
340	345	350
Asn Arg Val Thr His Ile Leu Asn Met Ala Arg Glu Ile Asp Asn Phe		
355	360	365
Tyr Pro Glu Arg Phe Thr Tyr His Asn Val Arg Leu Trp Asp Glu Glu		
370	375	380
Ser Ala Gln Leu Leu Pro His Trp Lys Glu Thr His Arg Phe Ile Glu		
385	390	395
Ala Ala Arg Ala Gln Gly Thr His Val Leu Val His Cys Lys Met Gly		
405	410	415
Val Ser Arg Ser Ala Ala Thr Val Leu Ala Tyr Ala Met Lys Gln Tyr		
420	425	430
Glu Cys Ser Leu Glu Gln Ala Leu Arg His Val Gln Glu Leu Arg Pro		
435	440	445
Ile Ala Arg Pro Asn Pro Gly Phe Leu Arg Gln Leu Gln Ile Tyr Gln		
450	455	460
Gly Ile Leu Thr Ala Ser Arg Gln Ser His Val Trp Glu Gln Lys Val		
465	470	475
Gly Gly Val Ser Pro Glu Glu His Pro Ala Pro Glu Val Ser Thr Pro		
485	490	495
Phe Pro Pro Leu Pro Pro Glu Pro Glu Gly Gly Glu Glu Lys Val		
500	505	510
Val Gly Met Glu Glu Ser Gln Ala Pro Lys Glu Glu Pro Gly Pro		
515	520	525
Arg Pro Arg Ile Asn Leu Arg Gly Val Met Arg Ser Ile Ser Leu Leu		
530	535	540
Glu Pro Ser Leu Glu Leu Glu Ser Thr Ser Glu Thr Ser Asp Met Pro		
545	550	555
Glu Val Phe Ser Ser His Glu Ser Ser His Glu Glu Pro Leu Gln Pro		
565	570	575
Phe Pro Gln Leu Ala Arg Thr Lys Gly Gly Gln Gln Val Asp Arg Gly		
580	585	590
Pro Gln Pro Ala Leu Lys Ser Arg Gln Ser Val Val Thr Leu Gln Gly		
595	600	605
Ser Ala Val Val Ala Asn Arg Thr Gln Ala Phe Gln Glu Gln Glu Gln		
610	615	620
Gly Gln Gly Gln Gly Gln Gly Glu Pro Cys Ile Ser Ser Thr Pro Arg		
625	630	635
Phe Arg Lys Val Val Arg Gln Ala Ser Val His Asp Ser Gly Glu Glu		
645	650	655
Gly Glu Ala		

<210> 137
 <211> 1416
 <212> DNA
 <213> Mus musculus

<400> 137
 atggccctgg tcacagtgg ccgttcgccc ccgggcagcg gcgcctccac gcccgtaggg 60

```

ccctgggacc aggcgggtcca gcgaaggagt cgactccagc gaaggcagag ctttgcggtg 120
ctccgtgggg ctgtcctggg actgcaggat ggaggggaca atgatgatgc agcagaggcc 180
agttctgagc caacagagaa ggccccgagt gaggaggagc tccacgggga ccagacagac 240
ttcgggcaag gatcccagag tccccagaag caggaggagc agaggcagca cctgcacctc 300
atggtacagc tgctgaggcc gcaggatgac atccgcctgg cagcccagct ggaggcaccc 360
cggcctcccc ggtcccgcta cctgctggta gtttctacac gagaaggaga aggtctgagc 420
caggatgaga cggctcctct gggcgtggat ttccctgaca gcagctcccc cagctgcacc 480
ctgggcctgg tcttgccctt ctggagtgc acccaggtgt acttagatgg agacgggggc 540
ttcagcgtga cgtctggtgg gcaaagccgg atcttcaagc ccatctccat ccagaccatg 600
tgggccacac tccaggtatt gcaccaagca tgtgaggcag ctctaggcag cggccttgta 660
ccgggtggca gtgcctcac ctgggccagc cactaccagg agagactgaa ctccgaacag 720
agctgectca atgagtggac ggctatggcc gacctggagt ctctgcggcc tcccagcgcc 780
gagcctggcg ggtcctcaga acaggagcag atggagcagg cgatccgtgc tgagctgtgg 840
aaagtgttgg atgtcagtga cctggagagt gtcaactcca aagagatccg ccaggctctg 900
gagctgcgcc tggggctccc cctccagcag taccgtgact tcatcgacaa ccagatgctg 960
ctgctggtgg cacagcggga ccgagcctcc cgcacttccc cccacctcta cctgggctca 1020
gagtggaaac cagcaaactt ggaggagctg cagaggaaca gggtcaccca catcttgaac 1080
atggcccggg agattgacaa cttctacctt gagcgcttca cctaccacaa tgtgcgcctc 1140
tgggatgagg agtcggccca gctgctgccc cactggaagg agacgcaccg cttcattgag 1200
gctgcaagag cacagggcac ccacgtgctg gtccactgca agatgggcgt cagccgctca 1260
gcggccacag tgctggccta tgccatgaag cagtacgaat gcagcctgga gcaggccctg 1320
cgccacgtgc aggagctccg gcccatcgcc cgccccaacc ctggcttctt gcgccagctg 1380
cagatctacc agggcctcct gacggccaga acctga 1416

```

<210> 138

<211> 471

<212> PRT

<213> Mus musculus

<400> 138

```

Met Ala Leu Val Thr Val Ser Arg Ser Pro Pro Gly Ser Gly Ala Ser
 1           5           10          15
Thr Pro Val Gly Pro Trp Asp Gln Ala Val Gln Arg Arg Ser Arg Leu
 20          25          30
Gln Arg Arg Gln Ser Phe Ala Val Leu Arg Gly Ala Val Leu Gly Leu
 35          40          45
Gln Asp Gly Gly Asp Asn Asp Asp Ala Ala Glu Ala Ser Ser Glu Pro
 50          55          60
Thr Glu Lys Ala Pro Ser Glu Glu Glu Leu His Gly Asp Gln Thr Asp
 65          70          75          80
Phe Gly Gln Gly Ser Gln Ser Pro Gln Lys Gln Glu Glu Gln Arg Gln
 85          90          95
His Leu His Leu Met Val Gln Leu Leu Arg Pro Gln Asp Asp Ile Arg
100         105         110
Leu Ala Ala Gln Leu Glu Ala Pro Arg Pro Pro Arg Leu Arg Tyr Leu
115         120         125
Leu Val Val Ser Thr Arg Glu Gly Glu Gly Leu Ser Gln Asp Glu Thr
130         135         140
Val Leu Leu Gly Val Asp Phe Pro Asp Ser Ser Ser Pro Ser Cys Thr
145         150         155         160
Leu Gly Leu Val Leu Pro Leu Trp Ser Asp Thr Gln Val Tyr Leu Asp
165         170         175
Gly Asp Gly Gly Phe Ser Val Thr Ser Gly Gly Gln Ser Arg Ile Phe
180         185         190
Lys Pro Ile Ser Ile Gln Thr Met Trp Ala Thr Leu Gln Val Leu His
195         200         205
Gln Ala Cys Glu Ala Ala Leu Gly Ser Gly Leu Val Pro Gly Gly Ser
210         215         220

```

Ala Leu Thr Trp Ala Ser His Tyr Gln Glu Arg Leu Asn Ser Glu Gln
 225 230 235 240
 Ser Cys Leu Asn Glu Trp Thr Ala Met Ala Asp Leu Glu Ser Leu Arg
 245 250 255
 Pro Pro Ser Ala Glu Pro Gly Gly Ser Ser Glu Gln Glu Gln Met Glu
 260 265 270
 Gln Ala Ile Arg Ala Glu Leu Trp Lys Val Leu Asp Val Ser Asp Leu
 275 280 285
 Glu Ser Val Thr Ser Lys Glu Ile Arg Gln Ala Leu Glu Leu Arg Leu
 290 295 300
 Gly Leu Pro Leu Gln Gln Tyr Arg Asp Phe Ile Asp Asn Gln Met Leu
 305 310 315 320
 Leu Leu Val Ala Gln Arg Asp Arg Ala Ser Arg Ile Phe Pro His Leu
 325 330 335
 Tyr Leu Gly Ser Glu Trp Asn Ala Ala Asn Leu Glu Glu Leu Gln Arg
 340 345 350
 Asn Arg Val Thr His Ile Leu Asn Met Ala Arg Glu Ile Asp Asn Phe
 355 360 365
 Tyr Pro Glu Arg Phe Thr Tyr His Asn Val Arg Leu Trp Asp Glu Glu
 370 375 380
 Ser Ala Gln Leu Leu Pro His Trp Lys Glu Thr His Arg Phe Ile Glu
 385 390 395 400
 Ala Ala Arg Ala Gln Gly Thr His Val Leu Val His Cys Lys Met Gly
 405 410 415
 Val Ser Arg Ser Ala Ala Thr Val Leu Ala Tyr Ala Met Lys Gln Tyr
 420 425 430
 Glu Cys Ser Leu Glu Gln Ala Leu Arg His Val Gln Glu Leu Arg Pro
 435 440 445
 Ile Ala Arg Pro Asn Pro Gly Phe Leu Arg Gln Leu Gln Ile Tyr Gln
 450 455 460
 Gly Ile Leu Thr Ala Arg Thr
 465 470

<210> 139
 <211> 3496
 <212> DNA
 <213> Homo sapiens

<400> 139
 gagagaagga gaagataata tactgaaaag aagaggagga ggagagcgac gggacgggac 60
 gcgagcggga gcgcagccgc cctctcggt cgcggcggc gcctcgcaag tccgggaggc 120
 gaggggggccc cgaggggaga cgccgtgaca actttcggtt ccctctgagg gaattgggag 180
 gtcggcgggc ccaaaagctt tcagtcaggt gtaaagctgt tggagcgagg gagcaaaggt 240
 aaagaatgat gtaatgcgct ggctgctcca aagcatcttt tgttggtgaa tggttattcc 300
 agtcatctct ttaataatca aatgtgagg gctgctttgt ggacggagtc ctttgcaaga 360
 gcacatcaac gggaaagaga aagagacatt cacttgagg gctcttgctg aaaatgggtt 420
 taactctcct tttgccagtc accaccagcc tgacctcata cacttttagt acaatggagt 480
 ggctgagcct ttgagcacac caccattaca tcatcggtgc aaattaaaga aggaggtggg 540
 aaaagaggac ttattgttgt catggcccat gagatgattg gaactcaaat tgttactgag 600
 aggttggttg ctctgctgga aagtgaacg gaaaaagtgc tgctaattga tagccggcca 660
 tttgtggaat acaatacatc ccacattttg gaagccatta atatcaactg ctccaagctt 720
 atgaagcgaa ggttgcaaca ggacaaagt ttaattacag agctcatcca gcattcagcg 780
 aaacataagg ttgacattga ttgcagtcag aaggttgtag ttacgatca aagctcccaa 840
 gatgttgctt ctctctcttc agactgtttt ctactgtac ttctgggtaa actggagaag 900
 agcttcaact ctgttcacct gcttgagggt gggtttgctg agttctctcg ttgtttccct 960
 ggctctgtg aaggaaaatc cactctagtc cctacctgca tttctcagcc ttgcttacct 1020
 gttgccaaaca ttggggccaac ccgaattctt cccaatcttt atcttggctg ccagcgagat 1080

```

gtcctcaaca aggagctgat gcagcagaat gggatttggtt atgtgtttaa tgccagcaat 1140
acctgtccaa agcctgactt tatccccgag tctcatttcc tgcgtgtgcc tgtgaatgac 1200
agctttttgtg agaaaatttt gccgtgggtg gacaaatcag tagatttcat tgagaaagca 1260
aaagcctcca atggatgtgt tctagtgcac tgttttagctg ggatctcccg ctccgccacc 1320
atcgctatcg cctacatcat gaagaggatg gacatgtctt tagatgaagc ttacagattt 1380
gtgaaagaaa aaagacctac tatatctcca aacttcaatt ttctggggcca actcctggac 1440
tatgagaaga agattaagaa ccagactgga gcatcagggc caaagagcaa actcaagctg 1500
ctgcacctgg agaagccaaa tgaacctgtc cctgctgtct cagagggtgg acagaaaagc 1560
gagacgcccc tcagtcacc ctgtgccgac tctgtacct cagaggcagc aggacaaagg 1620
cccgtgcac ccgccagcgt gcccagcgtg cccagcgtgc agccgtcgt gtttagaggac 1680
agcccgttg tacaggcgt cagtgggctg cacctgtccg cagacaggct ggaagacagc 1740
aataagctca agcgttccct ctctctggat atcaaatcag ttcatattc agccagcatg 1800
gcagcatcct tacatggctt ctctcatca gaagatgctt tggaatacta caaaccttcc 1860
actactctgg atgggaccaa caagctatgc cagttctccc ctgttcagga actatcgag 1920
cagactcccg aaaccagtcc tgataaggag gaagccagca tcccaagaa gctgcagacc 1980
gccaggcctt cagacagcca gagcaagcga ttgcattcgg tcagaaccag cagcagtggc 2040
accgccaga ggtccctttt atctccactg catcgaagtg ggagcgtgga ggacaattac 2100
cacaccagct tcccttttcg cttttccacc agccagcagc acctcacgaa gtctgctggc 2160
ctgggcctta agggctggca ctggatata ttggccccc agacctctac ccttccctg 2220
accagcagct ggtattttgc cacagagtcc tcacacttct actctgctc agccatctac 2280
ggaggcagtg ccagttactc tgcctacagc tgcagccagc tgcccacttg cggagaccaa 2340
gtctattctg tgcgcaggcg gcagaagcca agtgacagag ctgactcgcg gcggagctgg 2400
catgaagaga gcccctttga aaagcagttt aaacgcagaa gctgccaaat ggaatttgga 2460
gagagcatca tgtcagagaa caggtcacgg gaagagctgg ggaaagtggg cagtcagtct 2520
agcttttcgg gcagcatgga aatcattgag gtctcctgag aagaaagaca cttgtgactt 2580
ctatagacaa ttttttttct ttgttcacaa aaaaattccc tgtaaactctg aaatatatat 2640
atgtacatac atatatattt ttggaaaatg gagctatggt gtaaaagcaa caggtggatc 2700
aaccagttg ttactctctt aacatctgca tttgagagat cagctaatac ttctctcaac 2760
aaaaatggaa gggcagatgc tagaatcccc cctagacgga ggaaaaccat tttattcagt 2820
gaattacaca tctctctgtt cttaaaaaag caagtgtctt tgggtgttga ggacaaaatc 2880
cctaccatt ttccacgttg tgcactaag agatctcaaa tattagtctt tgtccggacc 2940
cttccatagt acaccttagc gctgagactg agccagcttg ggggtcaggt aggtagacct 3000
tgttagggac agagcctagt ggtaaatcca agagaaatga tccatccaa agctgattca 3060
caaaccacg ctacactgac agccgagggg cacgagcatc actctgctgg acggaccatt 3120
aggggccttg ccaaggctca ccttagagca aaccagtac ctcagacagg aaagtcgggg 3180
ctttgaccac taccatatct ggtagcccat tttctaggca ttgtgaatag gtaggtagct 3240
agtcacactt ttcagaccaa ttcaaactgt ctatgcacaa aattcccgtg ggcctagatg 3300
gagataattt ttttttcttc tcagctttat gaagagaagg gaaactgtct aggattcagc 3360
tgaaccacca ggaacctggc aacatcacga ttttaagctaa ggttgggagg ctaacgagtc 3420
tacctccctc tttgtaaatc aaagaattgt ttaaatggg attgtcaatc ctttaaataa 3480
agatgaactt ggtttc 3496

```

<210> 140
 <211> 665
 <212> PRT
 <213> Homo sapiens

<400> 140
 Met Ala His Glu Met Ile Gly Thr Gln Ile Val Thr Glu Arg Leu Val
 1 5 10 15
 Ala Leu Leu Glu Ser Gly Thr Glu Lys Val Leu Leu Ile Asp Ser Arg
 20 25 30
 Pro Phe Val Glu Tyr Asn Thr Ser His Ile Leu Glu Ala Ile Asn Ile
 35 40 45
 Asn Cys Ser Lys Leu Met Lys Arg Arg Leu Gln Gln Asp Lys Val Leu
 50 55 60
 Ile Thr Glu Leu Ile Gln His Ser Ala Lys His Lys Val Asp Ile Asp
 65 70 75 80

Cys	Ser	Gln	Lys	Val	Val	Val	Tyr	Asp	Gln	Ser	Ser	Gln	Asp	Val	Ala	
				85					90					95		
Ser	Leu	Ser	Ser	Asp	Cys	Phe	Leu	Thr	Val	Leu	Leu	Gly	Lys	Leu	Glu	
			100					105					110			
Lys	Ser	Phe	Asn	Ser	Val	His	Leu	Leu	Ala	Gly	Gly	Phe	Ala	Glu	Phe	
		115					120					125				
Ser	Arg	Cys	Phe	Pro	Gly	Leu	Cys	Glu	Gly	Lys	Ser	Thr	Leu	Val	Pro	
	130					135					140					
Thr	Cys	Ile	Ser	Gln	Pro	Cys	Leu	Pro	Val	Ala	Asn	Ile	Gly	Pro	Thr	
145				150						155					160	
Arg	Ile	Leu	Pro	Asn	Leu	Tyr	Leu	Gly	Cys	Gln	Arg	Asp	Val	Leu	Asn	
				165					170						175	
Lys	Glu	Leu	Met	Gln	Gln	Asn	Gly	Ile	Gly	Tyr	Val	Leu	Asn	Ala	Ser	
			180					185					190			
Asn	Thr	Cys	Pro	Lys	Pro	Asp	Phe	Ile	Pro	Glu	Ser	His	Phe	Leu	Arg	
		195					200					205				
Val	Pro	Val	Asn	Asp	Ser	Phe	Cys	Glu	Lys	Ile	Leu	Pro	Trp	Leu	Asp	
	210					215					220					
Lys	Ser	Val	Asp	Phe	Ile	Glu	Lys	Ala	Lys	Ala	Ser	Asn	Gly	Cys	Val	
225				230						235					240	
Leu	Val	His	Cys	Leu	Ala	Gly	Ile	Ser	Arg	Ser	Ala	Thr	Ile	Ala	Ile	
				245					250					255		
Ala	Tyr	Ile	Met	Lys	Arg	Met	Asp	Met	Ser	Leu	Asp	Glu	Ala	Tyr	Arg	
			260				265						270			
Phe	Val	Lys	Glu	Lys	Arg	Pro	Thr	Ile	Ser	Pro	Asn	Phe	Asn	Phe	Leu	
		275					280					285				
Gly	Gln	Leu	Leu	Asp	Tyr	Glu	Lys	Lys	Ile	Lys	Asn	Gln	Thr	Gly	Ala	
	290					295					300					
Ser	Gly	Pro	Lys	Ser	Lys	Leu	Lys	Leu	Leu	His	Leu	Glu	Lys	Pro	Asn	
305				310						315					320	
Glu	Pro	Val	Pro	Ala	Val	Ser	Glu	Gly	Gly	Gln	Lys	Ser	Glu	Thr	Pro	
				325					330					335		
Leu	Ser	Pro	Pro	Cys	Ala	Asp	Ser	Ala	Thr	Ser	Glu	Ala	Ala	Gly	Gln	
			340					345					350			
Arg	Pro	Val	His	Pro	Ala	Ser	Val	Pro	Ser	Val	Pro	Ser	Val	Gln	Pro	
		355					360					365				
Ser	Leu	Leu	Glu	Asp	Ser	Pro	Leu	Val	Gln	Ala	Leu	Ser	Gly	Leu	His	
	370					375					380					
Leu	Ser	Ala	Asp	Arg	Leu	Glu	Asp	Ser	Asn	Lys	Leu	Lys	Arg	Ser	Phe	
385				390						395					400	
Ser	Leu	Asp	Ile	Lys	Ser	Val	Ser	Tyr	Ser	Ala	Ser	Met	Ala	Ala	Ser	
				405					410					415		
Leu	His	Gly	Phe	Ser	Ser	Ser	Glu	Asp	Ala	Leu	Glu	Tyr	Tyr	Lys	Pro	
		420						425					430			
Ser	Thr	Thr	Leu	Asp	Gly	Thr	Asn	Lys	Leu	Cys	Gln	Phe	Ser	Pro	Val	
		435					440					445				
Gln	Glu	Leu	Ser	Glu	Gln	Thr	Pro	Glu	Thr	Ser	Pro	Asp	Lys	Glu	Glu	
	450					455					460					
Ala	Ser	Ile	Pro	Lys	Lys	Leu	Gln	Thr	Ala	Arg	Pro	Ser	Asp	Ser	Gln	
465				470						475					480	
Ser	Lys	Arg	Leu	His	Ser	Val	Arg	Thr	Ser	Ser	Ser	Gly	Thr	Ala	Gln	
				485					490					495		
Arg	Ser	Leu	Leu	Ser	Pro	Leu	His	Arg	Ser	Gly	Ser	Val	Glu	Asp	Asn	
			500					505					510			
Tyr	His	Thr	Ser	Phe	Leu	Phe	Gly	Leu	Ser	Thr	Ser	Gln	Gln	His	Leu	
		515					520					525				
Thr	Lys	Ser	Ala	Gly	Leu	Gly	Leu	Lys	Gly	Trp	His	Ser	Asp	Ile	Leu	
	530					535						540				

Ala Pro Gln Thr Ser Thr Pro Ser Leu Thr Ser Ser Trp Tyr Phe Ala
 545 550 555 560
 Thr Glu Ser Ser His Phe Tyr Ser Ala Ser Ala Ile Tyr Gly Gly Ser
 565 570 575
 Ala Ser Tyr Ser Ala Tyr Ser Cys Ser Gln Leu Pro Thr Cys Gly Asp
 580 585 590
 Gln Val Tyr Ser Val Arg Arg Arg Gln Lys Pro Ser Asp Arg Ala Asp
 595 600 605
 Ser Arg Arg Ser Trp His Glu Glu Ser Pro Phe Glu Lys Gln Phe Lys
 610 615 620
 Arg Arg Ser Cys Gln Met Glu Phe Gly Glu Ser Ile Met Ser Glu Asn
 625 630 635 640
 Arg Ser Arg Glu Glu Leu Gly Lys Val Gly Ser Gln Ser Ser Phe Ser
 645 650 655
 Gly Ser Met Glu Ile Ile Glu Val Ser
 660 665

<210> 141
 <211> 3332
 <212> DNA
 <213> Homo sapiens

<400> 141
 gagagaagga gaagataata tactgaaaag aagaggagga ggagagcgac gggacgggac 60
 gcgagcggga ggcagccgc cctctcggt cgcgcggcgc gcctcgcaag tccgggaggc 120
 gaggggggccc cgaggggaga cgcctgaca actttcggtt ccctctgagg gaattgggag 180
 gtgcgcggccc ccaaaagctt tcagtccagt gtaaaagctgt tggagcgcgg gagcaaaggt 240
 aaagaatgat gtaatgcgct ggctgctcca aagcatcttt tgttgggaa tggttattcc 300
 agtcatctct ttatgaatca aatgtgaggy gctgctttgt ggacggagtc ctttgcaaga 360
 gcacatcaac gggaaagaga aagagacatt cacttggagg gctcttgctg aaaatgggtt 420
 taactctctt tttgccagtc accaccagcc tgacctcata cacttttagt acaatggagt 480
 ggctgagcct ttgagcacac caccattaca tcatcgtagc aaattaaaga aggaggtggg 540
 aaaagaggac ttattgttgt catggcccat gagatgattg gaactcaaat tgttactgag 600
 aggttggttg ctctgctgga aagtggaaag gaaaaagtgc tgctaattga tagccggcca 660
 tttgtggaat acaatacatc ccacattttg gaagccatta atatcaactg ctccaagctt 720
 atgaagcgaa ggttgcaaca ggacaaagtg ttaattacag agtcatcca gcattcagcg 780
 aaacataagg ttgacattga ttgcagtcag aaggtttagt tttacgatca aagctcccaa 840
 gatgttgccct ctctctcttc agactgtttt ctcactgtac ttctgggtaa actggagaag 900
 agcttcaact ctgttcacct gcttgagga gctgatgcag cagaatggga ttggttatgt 960
 gttaaagtgc agcaatacct gtccaaagcc tgactttatc cccgagtctc atttcctgctg 1020
 tgtgcctgtg aatgacagct tttgtgagaa aattttgccc tggttggaca aatcagtaga 1080
 tttcattgag aaagcaaaag cctccaatgg atgtgttcta gtgcactgtt tagctgggat 1140
 ctcccgtccc gccaccatcg ctatcgcta catcatgaag aggatggaca tgtctttaga 1200
 tgaagcttac agatttgtga aagaaaaaag acctactata tctccaaact tcaattttct 1260
 gggccaactc ctggactatg agaagaagat taagaaccag actggagcat cagggccaaa 1320
 gagcaaactc aagctgctgc acctggagaa gccaaatgaa cctgtccctg ctgtctcaga 1380
 ggggtggacag aaaagcgaga cgccccctag tccacctgt gccgactctg ctacctcaga 1440
 ggcagcagga caaaggcccg tgcattcccg cagcgtgccc agcgtgcccc gcgtgcagcc 1500
 gtgcgtgtta gaggacagcc cgctgggtaca ggcgtcaggt gggctgcacc tgtccgcaga 1560
 caggctggaa gacagcaata agctcaagcg ttcttctct ctggatatca aatcagtttc 1620
 atattcagcc agcatggcag catccttaca tggcttctcc tcatcagaag atgctttgga 1680
 atactacaaa ccttccacta ctctggatgg gaccaacaag ctatgccagt tctcccctgt 1740
 tcaggaacta tcggagcaga ctcccgaaac cagtctgat aaggaggaag ccagcatccc 1800
 caagaagctg cagaccgcca ggccttcaga cagccagagc aagcgattgc attcggtcag 1860
 aaccagcagc agtggcaccg ccagagggtc ccttttatct ccaactgcac gaagtgggag 1920
 cgtggaggac aattaccaca ccagcttctt tttcggcctt tccaccagcc agcagcacct 1980
 cacgaagtct gctggcctgg gccttaagggt ctggcactcg gatattcttg ccccccagac 2040

```

ctctaccctt tccctgacca gcagctggta ttttgccaca gagtcctcac acttctactc 2100
tgccctcagcc atctacggag gcagtgccag ttactctgcc tacagctgca gccagctgcc 2160
cacttgccga gaccaagtct attctgtgcg caggcggcag aagccaagtg acagagctga 2220
ctcgcggcgg agctggcatg aagagagccc ctttgaaaag cagtttaaac gcagaagctg 2280
ccaaatggaa tttggagaga gcatcatgtc agagaacagg tcacgggaag agctggggaa 2340
agtgggcagt cagtctagct tttcgggcag catggaaatc attgaggtct cctgagaaga 2400
aagacacttg tgacttctat agacaatttt tttttcttgt tcacaaaaaa attccctgta 2460
aatctgaaat atatatatgt acatacatat atatttttgg aaaatggagc tatggtgtaa 2520
aagcaacagg tggatcaacc cagttgttac tctcttaaca tctgcatttg agagatcagc 2580
taatacttct ctcaacaaaa atggaagggc agatgctaga atcccccta gacggaggaa 2640
aaccatttta ttcagtgaat tacacatcct cttgttctta aaaaagcaag tgtctttggt 2700
gttgaggac aaaatccctt accattttcc acgttgtgct actaagagat ctcaaatt 2760
agtctttgtc cggacccttc catagtacac cttagcgtg agactgagcc agcttggggg 2820
tcaggtaggt agaccctgtt agggacagag cctagtggta aatccaagag aaatgatcct 2880
atccaaagct gattcacaaa cccacgtca cctgacagcc gagggacacg agcatcactc 2940
tgctggacgg accattaggg gccttgccaa ggtctacctt agagcaaacc cagtacctca 3000
gacaggaaag tcggggcttt gaccactacc atatctggta gccattttc taggcattgt 3060
gaataggtag gtagctagtc acacttttca gaccaattca aactgtctat gcacaaaatt 3120
cccgtgggcc tagatggaga taattttttt ttcttctcag ctttatgaag agaagggaaa 3180
ctgtctagga ttcagctgaa ccaccaggaa cctggcaaca tcacgattta agctaagggt 3240
gggaggctaa cgagtctacc tccctctttg taaatcaaag aattgtttta aatgggattg 3300
tcaatccttt aaataaagat gaacttggtt tc 3332

```

<210> 142

<211> 517

<212> PRT

<213> Homo sapiens

<400> 142

```

Met Leu Pro Leu Ser Leu Gln Thr Val Phe Ser Leu Tyr Phe Trp Val
 1          5          10          15
Asn Trp Arg Arg Ala Ser Thr Leu Phe Thr Cys Leu Gln Glu Leu Met
      20          25          30
Gln Gln Asn Gly Ile Gly Tyr Val Leu Asn Ala Ser Asn Thr Cys Pro
      35          40          45
Lys Pro Asp Phe Ile Pro Glu Ser His Phe Leu Arg Val Pro Val Asn
 50          55          60
Asp Ser Phe Cys Glu Lys Ile Leu Pro Trp Leu Asp Lys Ser Val Asp
65          70          75          80
Phe Ile Glu Lys Ala Lys Ala Ser Asn Gly Cys Val Leu Val His Cys
      85          90          95
Leu Ala Gly Ile Ser Arg Ser Ala Thr Ile Ala Ile Ala Tyr Ile Met
      100          105          110
Lys Arg Met Asp Met Ser Leu Asp Glu Ala Tyr Arg Phe Val Lys Glu
      115          120          125
Lys Arg Pro Thr Ile Ser Pro Asn Phe Asn Phe Leu Gly Gln Leu Leu
      130          135          140
Asp Tyr Glu Lys Lys Ile Lys Asn Gln Thr Gly Ala Ser Gly Pro Lys
145          150          155          160
Ser Lys Leu Lys Leu Leu His Leu Glu Lys Pro Asn Glu Pro Val Pro
      165          170          175
Ala Val Ser Glu Gly Gly Gln Lys Ser Glu Thr Pro Leu Ser Pro Pro
      180          185          190
Cys Ala Asp Ser Ala Thr Ser Glu Ala Ala Gly Gln Arg Pro Val His
      195          200          205
Pro Ala Ser Val Pro Ser Val Pro Ser Val Gln Pro Ser Leu Leu Glu
      210          215          220
Asp Ser Pro Leu Val Gln Ala Leu Ser Gly Leu His Leu Ser Ala Asp

```

225		230		235		240
Arg Leu Glu Asp	Ser Asn Lys Leu Lys	Arg Ser Phe Ser Leu Asp	Ile			
	245	250	255			
Lys Ser Val Ser Tyr	Ser Ala Ser Met	Ala Ala Ser Leu His Gly	Phe			
	260	265	270			
Ser Ser Ser Glu Asp	Ala Leu Glu Tyr Tyr	Lys Pro Ser Thr Thr	Leu			
	275	280	285			
Asp Gly Thr Asn Lys	Leu Cys Gln Phe Ser	Pro Val Gln Glu Leu	Ser			
	290	295	300			
Glu Gln Thr Pro Glu	Thr Ser Pro Asp Lys	Glu Glu Ala Ser Ile	Pro			
305	310	315	320			
Lys Lys Leu Gln Thr	Ala Arg Pro Ser Asp	Ser Gln Ser Lys Arg	Leu			
	325	330	335			
His Ser Val Arg Thr	Ser Ser Ser Gly Thr	Ala Gln Arg Ser Leu	Leu			
	340	345	350			
Ser Pro Leu His Arg	Ser Gly Ser Val Glu	Asp Asn Tyr His Thr	Ser			
	355	360	365			
Phe Leu Phe Gly Leu	Ser Thr Ser Gln Gln	His Leu Thr Lys Ser	Ala			
	370	375	380			
Gly Leu Gly Leu Lys	Gly Trp His Ser Asp	Ile Leu Ala Pro Gln	Thr			
385	390	395	400			
Ser Thr Pro Ser Leu	Thr Ser Ser Trp Tyr	Phe Ala Thr Glu Ser	Ser			
	405	410	415			
His Phe Tyr Ser Ala	Ser Ala Ile Tyr Gly	Gly Ser Ala Ser Tyr	Ser			
	420	425	430			
Ala Tyr Ser Cys Ser	Gln Leu Pro Thr Cys	Gly Asp Gln Val Tyr	Ser			
	435	440	445			
Val Arg Arg Arg Gln	Lys Pro Ser Asp Arg	Ala Asp Ser Arg Arg	Ser			
	450	455	460			
Trp His Glu Glu Ser	Pro Phe Glu Lys Gln	Phe Lys Arg Arg Ser	Cys			
465	470	475	480			
Gln Met Glu Phe Gly	Glu Ser Ile Met Ser	Glu Asn Arg Ser Arg	Glu			
	485	490	495			
Glu Leu Gly Lys Val	Gly Ser Gln Ser Ser	Phe Ser Gly Ser Met	Glu			
	500	505	510			
Ile Ile Glu Val Ser						
	515					

<210> 143

<211> 1754

<212> DNA

<213> Homo sapiens

<400> 143

```

agaggcagag ggggtgggcgg gctggcccat ggctgagacc tctctcccag agctgggggg 60
agaggacaaa gccacgcctt gcccagcat cctggagctg gaggagctcc tgcgggcagg 120
gaagtcttct tgcagccgtg tggacgaagt ttggcccaac cttttcatag gagatgcggc 180
cacggcaaac aaccgctttg agctgtggaa gctgggcata acccacgtgc tgaacgccgc 240
ccacaagggc ctctactgtc agggcggccc tgactttctac ggcagcagtg tgagctacct 300
gggggtgccg gccacgacc tccctgattt tgacatcagt gcctacttct cctctgcggc 360
tgacttcata caccgtgcc tcaacacgcc tggggccaag gtctgtgtgc actgtgtggt 420
gggcgtgagc cgctctgcc cgctggtcct ggcctacctc atgctgcacc agcggctgtc 480
cctgcgccag gcggtgatca ccgtgaggca gcaccgatgg gtcttcccca accgaggctt 540
cctgcaccag ctctgcaggc tggaccagca actgcggggg gccggccaga gctgaggggc 600
cagagctggt ccttactccc tgccatgggg ctctgccact ttgccaccct ggcactgata 660
ctgctggtgc tgctggaggc tctggcccag gcggacacac agaagatggt ggaagcccag 720
cgtggggctg gccctagagc ctgctactcc atctggctcc tctggcgcc tacaccccct 780

```

```

ctcagccact gtcttcagtc tccacagaaa cagcatcaag tgtgcggaga caggcggctg 840
aaagccagca gcacgaactg cccgtcagag aagtgcacag cctgggccag atactcccac 900
aggatggact cactgcagaa gcaggacctc cggaggccca agatccatgg ggcagtccag 960
gcatctccct accagccgcc cacattggct tcgctgcagc gcttgctgtg ggtccgtcag 1020
gctgccacac tgaaccatat cgatgaggtc tggcccagcc tcttcctggg agatgcgtac 1080
gcagcccggg acaagagcaa gctgatccag ctgggaatca cccacgttgt gaatgccgt 1140
gcaggcaagt tccaggtgga cacaggtgcc aaattctacc gtggaatgtc cctggagtac 1200
tatggcatcg aggcggacga caacccttc ttcgacctca gtgtctactt tctgcctgtt 1260
gctcgataca tccgagctgc cctcagtgtt ccccaaggcc gcgtgctggt aactgtgcc 1320
atgggggtaa gccgctctgc cacacttgtc ctggccttcc tcatgatctg tgagaacatg 1380
acgctggtag aggccatcca gacggtgcag gccaccgca atatctgccc taactcaggc 1440
ttcctccggc agctccaggt tctggacaac cgactggggc gggagacggg gcggttctga 1500
tctggcaggc agccaggatc cctgaccctt ggcccaacc caccagcctg gccctgggaa 1560
cagcaggctc tgctgtttct agtgaccctg agatgtaaac agcaagtggg ggctgaggca 1620
gaggcaggga tagctgggtg gtgacctctt agcgggtgga tttccctgac ccaattcaga 1680
gattctttat gcaaaagtga gttcagtcca tctctataat aaaatattca tcgtcaaaaa 1740
aaaaaaaaaa aaaa 1754

```

<210> 144

<211> 188

<212> PRT

<213> Homo sapiens

<400> 144

```

Met Ala Glu Thr Ser Leu Pro Glu Leu Gly Gly Glu Asp Lys Ala Thr
1          5          10          15
Pro Cys Pro Ser Ile Leu Glu Leu Glu Leu Leu Arg Ala Gly Lys
20        25        30
Ser Ser Cys Ser Arg Val Asp Glu Val Trp Pro Asn Leu Phe Ile Gly
35        40        45
Asp Ala Ala Thr Ala Asn Asn Arg Phe Glu Leu Trp Lys Leu Gly Ile
50        55        60
Thr His Val Leu Asn Ala Ala His Lys Gly Leu Tyr Cys Gln Gly Gly
65        70        75        80
Pro Asp Phe Tyr Gly Ser Ser Val Ser Tyr Leu Gly Val Pro Ala His
85        90        95
Asp Leu Pro Asp Phe Asp Ile Ser Ala Tyr Phe Ser Ser Ala Ala Asp
100       105       110
Phe Ile His Arg Ala Leu Asn Thr Pro Gly Ala Lys Val Leu Val His
115       120       125
Cys Val Val Gly Val Ser Arg Ser Ala Thr Leu Val Leu Ala Tyr Leu
130       135       140
Met Leu His Gln Arg Leu Ser Leu Arg Gln Ala Val Ile Thr Val Arg
145       150       155       160
Gln His Arg Trp Val Phe Pro Asn Arg Gly Phe Leu His Gln Leu Cys
165       170       175
Arg Leu Asp Gln Gln Leu Arg Gly Ala Gly Gln Ser
180       185

```

<210> 145

<211> 1666

<212> DNA

<213> Homo sapiens

<400> 145

```

ggccccccgt tccccgccag gctgcaggcg tcgggcctgg gccgtcaggg cagctgtgac 60
cggatcgctt cccgggcggc gagctggggg tgcacccgga ccgcgcgcc cgggatcatg 120

```

```

ggcaatggca tgaccaaggt acttccctgga ctctacctcg gaaacttcat tgatgccaaa 180
gacctggatc agctggggccg aaataagatc acacacatca tctctatcca tgagtcaccc 240
cagcctctgc tgcaggatat cacctacctt cgcattcccg tcgctgatac ccttgaggta 300
cccatcaaaa agcacttcaa agaattgtat aacttcatcc actgctgccg ccttaatggg 360
gggaactgcc ttgtgcaactg ctttgcaggc atctctcgca gcaccacgat tgtgacagcg 420
tatgtgatga ctgtgacggg gctaggctgg cgggacgtgc ttgaagccat caaggccacc 480
aggcccatcg ccaaccccaa cccaggcttt aggcagcagc ttgaagagtt tggctggggc 540
agttcccaga aggggtgccag acataggacc tcaaaaacct ctgggtgccc atgccctccg 600
atgacttcag caacctggat ggtcacccga cccaaagtac cagatctgtc tgtgcttcgg 660
tgaggaggac cggggcccca cacagcacc caaggagcag ctcatcatgg cggacgtgca 720
ggtgcagctt cggcctggga gctcgtcctg cactctaagt gcctcaaccg agcgcccaga 780
tggttctcca acccctggca acccctgatg catcactcac cttcaatgca gctgcctcca 840
tcctaagcga gccgcttctt cttcttgtac ccgctgaagg cagcccccaa caggggggct 900
ccctactccc acccaacctt gccacacta agcccataga cttggggcct ccccggcac 960
atcaccagg tctgccggac ggcagaggtg gatcgcggcc ttccactcct ctgtcacggg 1020
gccccggaac tcgagagtag gccacaccgc ccccagctg ggcattggggc ttccggcagga 1080
aactgaactt gatcttgagg cccagaaaag gcagcaactg gagcagaagc aagacttcat 1140
ctcttgctga cagcccaatt tgtcaatagc gctttcttca gagccagcct taacctgctg 1200
ttgagtccat taaaacgttt gcttaaagtt tttaccaata attagatcat caggggttgtt 1260
tagtgtggga tcaagccata acaaaactgc ctacgctctc aggggcctag aatttacaga 1320
accttctctc tccttgcagc aagtctctct tctttattct gggggctggg aaggatccca 1380
aaacagggaa cttggccgaa ccctgggctt tggatgctaa ccactgaagt accagcacct 1440
gtaggatgct gtctttgaag aaactgaggc ggacctccaa atgcagccct aaggcagagg 1500
tcaacgtgga agaccagccc ttctccaagc cccactggtc tttgcaagct gtacgttgta 1560
ggcaatctga gaactggaaa gggggactac aaccagaaaag ttggttaccc tgccatggga 1620
ataaagtagc tgttttccac ccaaaaaaaa aaaaaaaaaa aaaaaa 1666

```

<210> 146

<211> 181

<212> PRT

<213> Homo sapiens

<400> 146

```

Met Gly Asn Gly Met Thr Lys Val Leu Pro Gly Leu Tyr Leu Gly Asn
1           5           10           15
Phe Ile Asp Ala Lys Asp Leu Asp Gln Leu Gly Arg Asn Lys Ile Thr
20           25           30
His Ile Ile Ser Ile His Glu Ser Pro Gln Pro Leu Leu Gln Asp Ile
35           40           45
Thr Tyr Leu Arg Ile Pro Val Ala Asp Thr Pro Glu Val Pro Ile Lys
50           55           60
Lys His Phe Lys Glu Cys Ile Asn Phe Ile His Cys Cys Arg Leu Asn
65           70           75           80
Gly Gly Asn Cys Leu Val His Cys Phe Ala Gly Ile Ser Arg Ser Thr
85           90           95
Thr Ile Val Thr Ala Tyr Val Met Thr Val Thr Gly Leu Gly Trp Arg
100          105          110
Asp Val Leu Glu Ala Ile Lys Ala Thr Arg Pro Ile Ala Asn Pro Asn
115          120          125
Pro Gly Phe Arg Gln Gln Leu Glu Glu Phe Gly Trp Ala Ser Ser Gln
130          135          140
Lys Gly Ala Arg His Arg Thr Ser Lys Thr Ser Gly Ala Gln Cys Pro
145          150          155          160
Pro Met Thr Ser Ala Thr Trp Met Val Thr Gly Pro Lys Val Pro Asp
165          170          175
Leu Ser Val Leu Arg
180

```

<210> 147
 <211> 1807
 <212> DNA
 <213> Homo sapiens

<400> 147

```

ggccccccgt tccccgccag gctgcaggcg tcgggcctgg gccgtcaggg cagctgtgac 60
cggatcgctt cccgggcggc gagctggggg tgcaccggga ccgcccggcc cgggatcatg 120
ggcaatggca tgaccaaggt acttcctgga ctctacctcg gaaacttcat tgatgcaaaa 180
gacctggatc agctggggcg aaataagatc acacacatca tctctatcca tgagtcaccc 240
cagcctctgc tgcaggatat cacctacctt cgcattcccg tcgctgatac ccctgaggta 300
cccatcaaaa agcacttcaa agaattgata aacttcatcc actgctgccg ccttaatggg 360
gggaactgcc ttgtgcaactg ctttgcaggc atctctcgca gcaccacgat tgtgacagcg 420
tatgtgatga ctgtgacggg gctaggctgg cgggacgtgc ttgaagccat caaggccacc 480
aggcccatcg ccaaccccaa cccaggcttt aggcagcagc ttgaagagtt tggctggggc 540
agttcccaga aggggtgccag acataggacc tcaaaaacct ctgggtgcca atgccctccg 600
atgacttcag caacctgcct gctggctgca cgtgtggctc ttctctccgc agcgtggtg 660
cggaagcca ccgggcgcac agcccagcgc tgtcgtctga gtccgcgggc ggccgcccag 720
cgctgctgg ggccgccacc tcacgttgca gcaggatggg caccggaccc aaagtaccag 780
atctgtctgt gcttcggtga ggaggaccg ggcccacac agcaccctaa ggagcagctc 840
atcatggcgg acgtgcaggt gcagcttcgg cctgggagct cgtcctgcac tctaagtgcc 900
tcaaccgagc gccagatgg gtctcaacc cctggcaacc ccgatggcat cactcacctt 960
caatgcagct gcctccatcc taagcgagcc gcttctctt cttgtaccg ctgaaggcag 1020
cccccaacag gggggctccc tactcccacc caacctgcc cactaagc ccatagactt 1080
ggggcctccc cggcggcaca tcaccaggt ctgccggacg gcagaggtgg atcgggcct 1140
tccactctc tgtcacgggg ccccggaact cgagagtagg ccacaccgcc cccagctgg 1200
gcatggggct tcggcaggaa actgaacttg atcttgaggc ccagaaaagg cagcaactgg 1260
agcagaagca agacttcata tcttgctgac agcccaattt gtcaatagcg ctttctctag 1320
agccagcctt aacctgctgt tgagctccatt aaaacgtttg cttaaagtth ttaccaataa 1380
ttagatcatc agggttgttt agtgtgggat caagccataa caaaactgcc tagcctctca 1440
ggggcctaga atttacagaa ccttctctct cctgcagct agtctctctt ctttattctg 1500
ggggctggga aggatcccaa aacagggaac ttggccgaac cctgggcttt ggatgctaac 1560
cactgaagta ccagcacctg taggatgctg tctttgaaga aactgaggcg gacctcaaaa 1620
tgcagcccta aggcagaggt caacgtggaa gaccagccct tctccaagcc ccactggtct 1680
ttgcaagctg tacgttgtag gcaatctgag aactggaaag ggggactaca accagaaagt 1740
tggttaccct gccatgggaa taaagtagct gttttccacc ccaaaaaaaaa aaaaaaaaaa 1800
aaaaaaa
1807

```

<210> 148
 <211> 298
 <212> PRT
 <213> Homo sapiens

<400> 148

```

Met Gly Asn Gly Met Thr Lys Val Leu Pro Gly Leu Tyr Leu Gly Asn
1           5           10          15
Phe Ile Asp Ala Lys Asp Leu Asp Gln Leu Gly Arg Asn Lys Ile Thr
20          25          30
His Ile Ile Ser Ile His Glu Ser Pro Gln Pro Leu Leu Gln Asp Ile
35          40          45
Thr Tyr Leu Arg Ile Pro Val Ala Asp Thr Pro Glu Val Pro Ile Lys
50          55          60
Lys His Phe Lys Glu Cys Ile Asn Phe Ile His Cys Cys Arg Leu Asn
65          70          75          80
Gly Gly Asn Cys Leu Val His Cys Phe Ala Gly Ile Ser Arg Ser Thr
85          90          95
Thr Ile Val Thr Ala Tyr Val Met Thr Val Thr Gly Leu Gly Trp Arg

```

	100		105		110
Asp Val	Leu Glu Ala Ile Lys	Ala Thr Arg Pro Ile Ala Asn Pro Asn			
	115	120		125	
Pro Gly	Phe Arg Gln Gln Leu Glu Glu Phe Gly Trp Ala Ser Ser Gln				
	130	135		140	
Lys Gly	Ala Arg His Arg Thr Ser Lys Thr Ser Gly Ala Gln Cys Pro				
145		150		155	160
Pro Met	Thr Ser Ala Thr Cys Leu Leu Ala Ala Arg Val Ala Leu Leu				
	165	170		175	
Ser Ala	Ala Leu Val Arg Glu Ala Thr Gly Arg Thr Ala Gln Arg Cys				
	180	185		190	
Arg Leu	Ser Pro Arg Ala Ala Ala Glu Arg Leu Leu Gly Pro Pro Pro				
	195	200		205	
His Val	Ala Ala Gly Trp Ser Pro Asp Pro Lys Tyr Gln Ile Cys Leu				
	210	215		220	
Cys Phe	Gly Glu Glu Asp Pro Gly Pro Thr Gln His Pro Lys Glu Gln				
225		230		235	240
Leu Ile	Met Ala Asp Val Gln Val Gln Leu Arg Pro Gly Ser Ser Ser				
	245	250		255	
Cys Thr	Leu Ser Ala Ser Thr Glu Arg Pro Asp Gly Ser Ser Thr Pro				
	260	265		270	
Gly Asn	Pro Asp Gly Ile Thr His Leu Gln Cys Ser Cys Leu His Pro				
	275	280		285	
Lys Arg	Ala Ala Ser Ser Ser Cys Thr Arg				
	290	295			

<210> 149
 <211> 1268
 <212> DNA
 <213> Homo sapiens

<400> 149
 ggccccccgt tccccgccag gctgcaggcg tcgggcctgg gccgtcaggg cagctgtgac 60
 cggatcgctt cccggggcgc gagctggggg tgcacccgga ccgccgcccc cgggatcatg 120
 ggcaatggca tgaccaagggt acttccctgga ctctacctcg gaaacttcat tgatgccaaa 180
 gacctggatc agctggggcg aaataagatc acacacatca tctctatcca tgagtcaccc 240
 cagcctctgc tgcaggatat cacctacctt cgcaccccgg tcgctgatac ccctgaggta 300
 cccatcaaaa agcacttcaa agaattgtatc aaacttcatcc actgctgccg ccttaattggg 360
 ggggaactgcc ttgtgcaactg ctttgcaggc atctctcgca gcaccacgat tgtgacagcg 420
 tatgtgatga ctgtgacggg gctaggctgg cgggacgtgc ttgaagccat caaggccacc 480
 aggcccatcg ccaaccccaa cccaggcttt aggcagcagc ttgaagagtt tggctggggc 540
 agttcccaga aggggtgccag acataggacc tcaaaaacct ctggtgcccc atgccctccg 600
 atgacttcag caacctggat ggtcaccgga cccaaagtac cagatctgtc tgtgcttcgg 660
 tgaggaggac ccggggccca cacagcacc caaggagcag ctcatcatgg cggacgtgca 720
 ggtgcagctt cggcctggga gctcgtcctg cactetaagt gcctcaaccg agcgcccaga 780
 tgggtcctca acccctggca accccgatgg catcactcac cttcaatgca gcttgccctc 840
 atcctaagcg agccgcttcc tcttcttgta cccgctgaag gcaagcccc aacagggggg 900
 ctccctactc ccaccaacc ctgccacac taagcccata gacttggggc ctccccggc 960
 acatcaccca ggtctgccg acggcagagg tggatcgcg ccttcactc ctctgtcacg 1020
 gggccccgga actcgagagt aggcctcacc gccccccagc tgggcatggg gcttcggcag 1080
 gaaactgaac ttgatcttga ggccagcaga aaggcagcaa ctggagcaga agcaagactt 1140
 catctcttgc tgacagccca atttgtcaat agcgttttcc tcagagccag ccttaacctg 1200
 ctgttgagtc cattaaaacg tttgcttaaa gtttttacca ataaaaaaaa aaaaaaaaaa 1260
 aaaaaaaaaa 1268

<210> 150
 <211> 181

<212> PRT
<213> Homo sapiens

<400> 150

```

Met Gly Asn Gly Met Thr Lys Val Leu Pro Gly Leu Tyr Leu Gly Asn
 1           5           10           15
Phe Ile Asp Ala Lys Asp Leu Asp Gln Leu Gly Arg Asn Lys Ile Thr
 20           25           30
His Ile Ile Ser Ile His Glu Ser Pro Gln Pro Leu Leu Gln Asp Ile
 35           40           45
Thr Tyr Leu Arg Ile Pro Val Ala Asp Thr Pro Glu Val Pro Ile Lys
 50           55           60
Lys His Phe Lys Glu Cys Ile Asn Phe Ile His Cys Cys Arg Leu Asn
 65           70           75           80
Gly Gly Asn Cys Leu Val His Cys Phe Ala Gly Ile Ser Arg Ser Thr
 85           90           95
Thr Ile Val Thr Ala Tyr Val Met Thr Val Thr Gly Leu Gly Trp Arg
 100          105          110
Asp Val Leu Glu Ala Ile Lys Ala Thr Arg Pro Ile Ala Asn Pro Asn
 115          120          125
Pro Gly Phe Arg Gln Gln Leu Glu Glu Phe Gly Trp Ala Ser Ser Gln
 130          135          140
Lys Gly Ala Arg His Arg Thr Ser Lys Thr Ser Gly Ala Gln Cys Pro
 145          150          155          160
Pro Met Thr Ser Ala Thr Trp Met Val Thr Gly Pro Lys Val Pro Asp
 165          170          175
Leu Ser Val Leu Arg
 180

```

<210> 151
<211> 1045
<212> DNA
<213> Homo sapiens

<400> 151

```

ggccccccgt tccccgccag gctgcaggcg tcgggcctgg gccgtcaggg cagctgtgac 60
cggatcgctt cccgggcggc gagctggggg tgcacccgga ccgccgccc cgggatcatg 120
ggcaatggca tgaccaaggt acttcttgga ctctacctcg gaaacttcat tgatgccaaa 180
gacctggatc agctgggccc aaataagatc acacacatca tctctatcca tgagtacccc 240
cagcctctgc tgcaggatat cacctacott cgcattcccg tcgctgatac ccctgaggta 300
cccatcaaaa agcaattcaa agaattgata aacttcatcc actgctgccg ccttaatggg 360
gggaactgcc ttgtgcaactg ctttgcaggc atctctcgca gcaccacgat tgtgacagcg 420
tatgtgatga ctgtgacggg gctaggctgg cgggacgtgc ttgaagccat caaggccacc 480
aggcccatcg ccaaccccaa cccaggcttt aggcagcagc ttgaagagtt tggctgggccc 540
agttcccaga aggggtgccag acataggacc tcaaaaacct ctggtgccca atgccctccg 600
atgacttcag caacctggat ggtcaccgga ccaaagtac cagatctgtc tgtgcttcgg 660
tgaggaggac ccgggcccac cacagcacc caaggagcag ctcatcatgg cggacctagt 720
ctctcttctt tattctgggg gctgggaagg atcccaaac agggaaacttg gccgaaccct 780
gggctttgga tgctaaccac tgaagtacca gcacctgtag gatgctgtct ttgaagaaac 840
tgaggcggaac ctccaaatgc agccctaagg cagagggtcaa cgtggaagac cagcccttct 900
ccaagcccca ctggtctttg caagctgtac gttgtaggca atctgagaac tggaaagggg 960
gactacaacc agaaagttag ttaccctgcc atgggaataa agtagctgtt ttccacccca 1020
taaaaaaaaa aaaaaaaaaa aaaaaa
1045

```

<210> 152
<211> 181
<212> PRT

<213> Homo sapiens

<400> 152

```

Met Gly Asn Gly Met Thr Lys Val Leu Pro Gly Leu Tyr Leu Gly Asn
 1           5           10           15
Phe Ile Asp Ala Lys Asp Leu Asp Gln Leu Gly Arg Asn Lys Ile Thr
 20           25           30
His Ile Ile Ser Ile His Glu Ser Pro Gln Pro Leu Leu Gln Asp Ile
 35           40           45
Thr Tyr Leu Arg Ile Pro Val Ala Asp Thr Pro Glu Val Pro Ile Lys
 50           55           60
Lys His Phe Lys Glu Cys Ile Asn Phe Ile His Cys Cys Arg Leu Asn
 65           70           75           80
Gly Gly Asn Cys Leu Val His Cys Phe Ala Gly Ile Ser Arg Ser Thr
 85           90           95
Thr Ile Val Thr Ala Tyr Val Met Thr Val Thr Gly Leu Gly Trp Arg
100           105           110
Asp Val Leu Glu Ala Ile Lys Ala Thr Arg Pro Ile Ala Asn Pro Asn
115           120           125
Pro Gly Phe Arg Gln Gln Leu Glu Glu Phe Gly Trp Ala Ser Ser Gln
130           135           140
Lys Gly Ala Arg His Arg Thr Ser Lys Thr Ser Gly Ala Gln Cys Pro
145           150           155           160
Pro Met Thr Ser Ala Thr Trp Met Val Thr Gly Pro Lys Val Pro Asp
165           170           175
Leu Ser Val Leu Arg
180

```

<210> 153

<211> 982

<212> DNA

<213> Homo sapiens

<400> 153

```

ggccccccgt tccccgccag gctgcaggcg tcgggcctgg gccgtcaggg cagctgtgac 60
cggatcgctt cccgggcggc gagctggggg tgcacccgga ccgccgcccc cgggatcatg 120
ggcaatggca tgaccaaggt acttcctgga ctctacctcg gaaacttcat tgatgcaaaa 180
gacctggatc agctggggccg aaataagatc acacacatca tctctatcca tgagtcaccc 240
cagcctctgc tgcaggatat cacctacct cgcaccccg tcgctgatac ccctgaggta 300
cccatcaaaa agcaacttcaa agaatgtatc aacttcatcc actgctgccg ccttaatggg 360
gggaactgcc ttgtgcaactg ctttgcaggc atctctcgca gcaccacgat tgtgacagcg 420
tatgtgatga ctgtgacggg gctaggctgg cgggacgtgc ttgaagccat caaggccacc 480
aggcccatcg ccaaccccaa cccaggcttt aggcagcagc ttaagagttt ggctgggcca 540
gttcccagaa ggatggtcac cggacccaaa gtaccagatc tgtctgtgct tcggtgagga 600
ggacccgggc cccacacagc accccaagga gcagctcatc atggcggacc tagtctctct 660
tctttattct gggggctggg aaggatccca aaacagggaa cttggccgaa ccttgggctt 720
tggatgctaa ccactgaagt accagcact gtaggatgct gtctttgaag aaactgaggc 780
ggacctccaa atgcagccct aaggcagagg tcaacgtgga agaccagccc ttctccaagc 840
ccactggtc tttgcaagct gtacgttgta ggcaatctga gaactggaaa gggggactac 900
aaccagaaag ttggttaccc tgccatggga ataaaagtagc tgttttccac cccccaaaaa 960
aaaaaaaaaa aaaaaaaaaa aa
982

```

<210> 154

<211> 159

<212> PRT

<213> Homo sapiens

<400> 154

```

Met Gly Asn Gly Met Thr Lys Val Leu Pro Gly Leu Tyr Leu Gly Asn
 1           5           10           15
Phe Ile Asp Ala Lys Asp Leu Asp Gln Leu Gly Arg Asn Lys Ile Thr
 20           25           30
His Ile Ile Ser Ile His Glu Ser Pro Gln Pro Leu Leu Gln Asp Ile
 35           40           45
Thr Tyr Leu Arg Ile Pro Val Ala Asp Thr Pro Glu Val Pro Ile Lys
 50           55           60
Lys His Phe Lys Glu Cys Ile Asn Phe Ile His Cys Cys Arg Leu Asn
 65           70           75           80
Gly Gly Asn Cys Leu Val His Cys Phe Ala Gly Ile Ser Arg Ser Thr
 85           90           95
Thr Ile Val Thr Ala Tyr Val Met Thr Val Thr Gly Leu Gly Trp Arg
 100          105          110
Asp Val Leu Glu Ala Ile Lys Ala Thr Arg Pro Ile Ala Asn Pro Asn
 115          120          125
Pro Gly Phe Arg Gln Gln Leu Lys Ser Leu Ala Gly Pro Val Pro Arg
 130          135          140
Arg Met Val Thr Gly Pro Lys Val Pro Asp Leu Ser Val Leu Arg
145          150          155

```

<210> 155

<211> 1064

<212> DNA

<213> Homo sapiens

<400> 155

```

ggccccccgt tccccgccag gctgcaggcg tcgggcctgg gccgtcaggg cagctgtgac 60
cggatcgctt cccgggcggc gagctggggg tgcaccggga ccgcccgcgc cgggatcatg 120
ggcaatggca tgaccaaggt acttcttgga ctctacctcg gaaacttcat tgatgccaaa 180
gacctggatc agctgggccc aaataagatc acacacatca tctctatcca tgagtcaccc 240
cagcctctgc tgcaggatat cacctacctt cgcateccgg tcgctgatac ccctgaggta 300
cccatcaaaa agcacttcaa agaatgtatc aacttcatcc actgctgccg ccttaatggg 360
gggaactgcc ttgtgcactg ctttgcaggc atctctcgca gcaccacgat tgtgacagcg 420
tatgtgatga ctgtgacggg gctaggctgg cgggacgtgc ttgaagccat caaggccacc 480
aggcccatcg ccaaccccaa cccaggcttt aggcagcagc ttgaagagtt tggctggggc 540
agttcccaga agggctttta ccaacctcat aagctgttgt gagaaccaat tgagacactg 600
caggaaagtg tttagccagg cccagcactg atgagcagtc ggatgggtcac cggacccaaa 660
gtaccagatc tgtctgtgct tcggtgagga ggaccggggc cccacacagc accccaagga 720
gcagctcatc atggcggacc tagtctctct tctttattct gggggctggg aaggatccca 780
aaacagggaa cttggccgaa ccctgggctt tggatgctaa ccaactgaagt accagcacct 840
gtaggatgct gtctttgaag aaactgaggc ggacctcaa atgcagccct aaggcagagg 900
tcaacgtgga agaccagccc ttctccaagc cccactggtc tttgcaagct gtacgttgta 960
ggcaatctga gaactggaaa gggggactac aaccagaaag ttggttaccg tgccatggga 1020
ataaagtagc tgttttccaa aaaaaaaaaa aaaaaaaaaa aaaa 1064

```

<210> 156

<211> 154

<212> PRT

<213> Homo sapiens

<400> 156

```

Met Gly Asn Gly Met Thr Lys Val Leu Pro Gly Leu Tyr Leu Gly Asn
 1           5           10           15
Phe Ile Asp Ala Lys Asp Leu Asp Gln Leu Gly Arg Asn Lys Ile Thr
 20           25           30

```

His Ile Ile Ser Ile His Glu Ser Pro Gln Pro Leu Leu Gln Asp Ile
 35 40 45
 Thr Tyr Leu Arg Ile Pro Val Ala Asp Thr Pro Glu Val Pro Ile Lys
 50 55 60
 Lys His Phe Lys Glu Cys Ile Asn Phe Ile His Cys Cys Arg Leu Asn
 65 70 75 80
 Gly Gly Asn Cys Leu Val His Cys Phe Ala Gly Ile Ser Arg Ser Thr
 85 90 95
 Thr Ile Val Thr Ala Tyr Val Met Thr Val Thr Gly Leu Gly Trp Arg
 100 105 110
 Asp Val Leu Glu Ala Ile Lys Ala Thr Arg Pro Ile Ala Asn Pro Asn
 115 120 125
 Pro Gly Phe Arg Gln Gln Leu Glu Glu Phe Gly Trp Ala Ser Ser Gln
 130 135 140
 Lys Gly Phe Tyr Gln Pro His Lys Leu Leu
 145 150

<210> 157
 <211> 833
 <212> DNA
 <213> Homo sapiens

<400> 157
 ggccccccgt tccccgccag gctgcaggcg tcgggcctgg gccgtcaggg cagctgtgac 60
 cggatcgctt cccgggcggc gagctggggg tgcacccgga ccgccgcccc cgggatcatg 120
 ggcaatggca tgaccaaggt acttcctgga ctctacctcg gaaacttcat tgatgccaaa 180
 gacctggatc agctgggccc aaataagatc acacacatca tctctatcca tgagtcaccc 240
 cagcctctgc tgcaggatat cacctacctt cgcctcccg tgcgtgatac cctgaggta 300
 cccatcaaaa agcacttcaa agaattgtatc aacttcatcc actgctgccg ccttaatggg 360
 gggaactgcc ttgtgcactg ctttgcaggg atctctcgca gcaccacgat tgtgacagcg 420
 tatgtgatga ctgtgacggg gctaggctgg cgggacgtgc ttgaagccat caaggccacc 480
 agggcccatc ccaaccccaa cccaggtttt aggcagcagc ttgaagagtt tggctggggc 540
 agttcccaga agcttcggcg gcagctggag gagecgttcg gcgagagccc cttccgcgac 600
 gaggaggagt tgcgcgcgt gctgccgctg tgcaagcgt gccggcaggg ctccgcgacc 660
 tcggcctcct ccgcggggcc gactcagca gcctccgagg gaaccgtgca gcgcctggtg 720
 ccgcgcacgc ccggggaagc ccaccggcgc ctgccgctgc tggcgcgcgt caagcagact 780
 ttctcttgcc tcccccggtg tctgtcccgc aagggcggca agtgaggatg cag 833

<210> 158
 <211> 235
 <212> PRT
 <213> Homo sapiens

<400> 158
 Met Gly Asn Gly Met Thr Lys Val Leu Pro Gly Leu Tyr Leu Gly Asn
 1 5 10 15
 Phe Ile Asp Ala Lys Asp Leu Asp Gln Leu Gly Arg Asn Lys Ile Thr
 20 25 30
 His Ile Ile Ser Ile His Glu Ser Pro Gln Pro Leu Leu Gln Asp Ile
 35 40 45
 Thr Tyr Leu Arg Ile Pro Val Ala Asp Thr Pro Glu Val Pro Ile Lys
 50 55 60
 Lys His Phe Lys Glu Cys Ile Asn Phe Ile His Cys Cys Arg Leu Asn
 65 70 75 80
 Gly Gly Asn Cys Leu Val His Cys Phe Ala Gly Ile Ser Arg Ser Thr
 85 90 95
 Thr Ile Val Thr Ala Tyr Val Met Thr Val Thr Gly Leu Gly Trp Arg

	100		105		110
Asp Val Leu Glu Ala Ile Lys Ala Thr Arg Pro Ile Ala Asn Pro Asn					
115		120		125	
Pro Gly Phe Arg Gln Gln Leu Glu Glu Phe Gly Trp Ala Ser Ser Gln					
130		135		140	
Lys Leu Arg Arg Gln Leu Glu Glu Arg Phe Gly Glu Ser Pro Phe Arg					
145		150		155	160
Asp Glu Glu Glu Leu Arg Ala Leu Leu Pro Leu Cys Lys Arg Cys Arg					
165		170		175	
Gln Gly Ser Ala Thr Ser Ala Ser Ser Ala Gly Pro His Ser Ala Ala					
180		185		190	
Ser Glu Gly Thr Val Gln Arg Leu Val Pro Arg Thr Pro Arg Glu Ala					
195		200		205	
His Arg Pro Leu Pro Leu Leu Ala Arg Val Lys Gln Thr Phe Ser Cys					
210		215		220	
Leu Pro Arg Cys Leu Ser Arg Lys Gly Gly Lys					
225		230		235	

<210> 159
 <211> 5117
 <212> DNA
 <213> Homo sapiens

<400> 159
 cccagccgc atgacgcgcg gaggaggcag cgggacgagc gcgggagccg ggaccgggta 60
 gccgcgcgc ggggggtgggc gccgctcgc cgcgcccgcg aagccctgc gcgctcaggg 120
 acgcggcccc cccgcggcag ccgcgctagg ctccggcgctg tggccgcggc cgcgcgcgcg 180
 ctgccatgtc tccggggaag ccggggcggg cggagcgggg acgaggcgga ccggctggcg 240
 gaggaggagg cgaaggagac ggcaggaggc ggcgacgacg gtgcccgggc tcgggcgcac 300
 ggcggggccc gattcgcgcg tccggggcac gtccaggggc gcgcggggca tgaagccggc 360
 ggcgcgggag gcgcggctgc ctccgcgctc gcccgggctg cgcggggcgc tgcgcgtgct 420
 gctgctgctg ctgcgcctgg gccagatcct gtgcgcaggt ggcacccta gtccaattcc 480
 tgacccttca gtagcaactg ttgccacagg ggaatggc ataacgcaga tcagcagtac 540
 agcagaatcc ttccataaac agaattgaac tggaaacact cagggtggaaa caaacaccag 600
 tgaggatggt gaaagctctg gagccaacga tagtttaaga acacctgaac aaggatctaa 660
 tgggactgat ggggcatctc aaaaaactcc cagtagcact gggcccagtc ctgtgtttga 720
 cattaaagct gtttccatca gtccaaccaa tgtgatctta acttgaaaaa gtaatgacac 780
 agctgcttct gagtacaagt atgtagtaaa gcataagatg gaaaatgaga agacaattac 840
 tgttgtgcat caaccatggt gtaacatcac aggcttacgt ccagcgactt catatgtatt 900
 ctccatcact ccaggaatag gcaatgagac ttggggagat ccagagtc taaaagtc 960
 cacagagccg atcccagttt ctgatctccg tgttgctcac ggggtgtgagg aaggctgctc 1020
 tctctcttgg agcaatggca atggcaccgc ctccctgccg gttcttcttg aaagcattgg 1080
 aagccatgag gagttgactc aagactcaag acttcaggtc aatatctcgg acctgaagcc 1140
 aggggttcaa tacaacatca acccgatatc tctacaatca aataagacaa agggagaccc 1200
 cttggcacag aagggtggctt ggatgccagc aatacagaga gaagccgggc agggagcccc 1260
 accgccccgt tgcgatgata gtcccttcgt gggacctgtg gaccatcct ccggccagca 1320
 gtcccagac acggaagtcc tgcttgctcg gtttagagcct ggcaccgat acaatggcac 1380
 cgtttattcc caagcagcga atggcacaga aggcagccc caggccatag agttcaggac 1440
 aaatgctatt cagggttttg acgtcaccgc tgtgaacatc agtgccacaa gcctgaccct 1500
 gatctggaaa gtcagcgata acgagtcgtc atctaactat acctacaaga tacatgtggc 1560
 gggggagaca gattcttcca atctcaacgt cagtgaacct cgcgctgtca tccccggact 1620
 ccgctccagc accttctaca acatcacagt gtgtcctgtc ctagggtgaca tcgagggcac 1680
 gccgggcttc ctccaagtgc acaccccccc tgttcagtt tctgacttcc gactgacagt 1740
 ggtagcagc acggagatcg gcttagcatg gagcagccat gatgcagaat catttcagat 1800
 gcatatcaca caggagggag ctggcaattc tcgggtagaa ataaccacca accaaagtat 1860
 tatcattggt ggcttggtcc ctggaaccaa gtattgcttt gaaatagttc caaaaggacc 1920
 aaatgggact gaaggggcat ctcgacagc ttgcaataga actgttccca gtgcagtggt 1980

tgacatccac	gtggtctacg	tcaccaccac	ggagatgtgg	ctggactgga	agagccctga	2040
cggtgcttcc	gagtatgtct	accatttagt	catagagtcc	aagcatggct	ctaaccacac	2100
aagcacgtat	gacaaagcga	ttactctcca	gggcctgatt	ccgggcacct	tatataacat	2160
caccatctct	ccagaagtgg	accacgtctg	gggggacccc	aactccactg	cacagtacac	2220
acggcccagc	aatgtgtcca	acattgatgt	aagtaccaac	accacagcag	caactttaag	2280
ttggcagaac	tttgatgacg	cctctcccac	gtactcctac	tgccttctta	ttgagaaggc	2340
tggaaattcc	agcaacgcaa	cacaagtagt	cacggacatt	ggaattactg	acgctacagt	2400
cactgaatta	atacctggct	catcatacac	agtggagctc	tttgacacaag	taggggatgg	2460
gatcaagtca	ctggaacctg	gccggaagtc	attctgtaca	gatcctgcgt	ccatggcctc	2520
cttcgactgc	gaagtggctc	ccaaagagcc	agccctgggt	ctcaaattga	cctgccctcc	2580
tggcgccaat	gcaggctttg	agctggagggt	cagcagtggg	gcctggaaca	atgcgaccac	2640
cctggagagc	tgctcctctg	agaatggcac	tgagtataga	acggaagtca	cgtattttga	2700
tttttctacc	togtacaaca	tcagcatcac	cactgtgtcc	tgtggaaaga	tggcagcccc	2760
cacccggaac	acctgcacta	ctggcatcac	agatccccct	cctccagatg	gatccccctaa	2820
tattacatct	gtcagtcaca	attcagtaaa	ggtaaggctc	agtggatttg	aagccagcca	2880
cggacccatc	aaagcctatg	ctgtcattct	caccaccggg	gaagctgggt	acccttctgc	2940
agatgtcctg	aaatacacgt	atgacgattt	caaaaaggga	gcctcagata	cttatgtgac	3000
atacctcata	agaacagaag	aaaaggggacg	ttctcagagc	ttgtctgaag	ttttgaaata	3060
tgaatttgac	gttggaatg	agtcaaccac	acttgggtat	tacaatggga	agctggaacc	3120
tctgggctcc	taccgggctt	gtgtggctgg	cttcaccaac	attaccttcc	accctcaaaa	3180
caaggggctc	attgatgggg	ctgagagcta	tgtgtccttc	agtcgctact	cagatgctgt	3240
ttccttgccc	caggatccag	gtgtcatctg	tggagcgggt	tttggctgta	tctttgggtg	3300
cctgggttatt	gtgactgtgg	gaggcttcat	cttctggaga	aagaagagga	aagatgcaaa	3360
gaataatgaa	gtgtcctttt	ctcaaattaa	acctaaaaaa	tctaagttaa	tcagagtggg	3420
gaatttttgag	gcctacttca	agaagcagca	agctgactcc	aactgtgggt	tcgcagagga	3480
atacgaagat	ctgaagcttg	ttggaattag	tcaacctaaa	tatgcagcag	aactggctga	3540
gaatagagga	aagaatcgct	ataataatgt	tctgccctat	gatatttccc	gtgtcaaaact	3600
ttcggctccag	acccattcaa	cggatgacta	catcaatgcc	aactacatgc	ctggctacca	3660
ctccaagaaa	gatttttattg	ccacacaagg	acctttaccg	aacactttga	aagatttttg	3720
gcgtatggtt	tgggagaaaa	atgtatatgc	catcattatg	ttgactaaat	gtgttgaaca	3780
gggaagaacc	aaatgtgagg	agtattggcc	ctccaagcag	gctcaggact	atggagacat	3840
aactgtggca	atgacatcag	aaattgttct	tccggaatgg	accatcagag	atttcacagt	3900
gaaaaatata	cagacaagtg	agagtcaccc	tctgagacag	ttccatttca	cctcctggcc	3960
agaccacggt	gttcccgaca	ccactgacct	gctcatcaac	ttccgggtacc	tcgttcgtga	4020
ctacatgaag	cagagtcttc	ccgaatcgcc	gattctgggt	cattgcagtg	ctgggggtcgg	4080
aaggacgggc	acttttcattg	ccattgatcg	tctcatctac	cagatagaga	atgagaacac	4140
cgtggatgtg	tatgggattg	tgtatgacct	togaatgcat	aggcctttaa	tgggtgcagac	4200
agaggaccag	tatgttttcc	tcaatcagtg	tgttttggat	attgtcagat	cccagaaaaga	4260
ctcaaaagta	gatcttatct	accagaacac	aactgcaatg	acaatctatg	aaaaccttgc	4320
gcccgtgacc	acattttggaa	agaccaatgg	ttacatcgcc	taattccaaa	ggaataacct	4380
ttctggagtg	aaccagaccg	tcgcacccac	agcgaaggca	catgccccga	tgtcgacatg	4440
tttttatatg	tctaatatct	taattctttg	ttctgttttg	tgagaactaa	ttttgagggc	4500
atgaagctgc	atatgataga	tgacaaattg	gggctgtcgg	gggctgtgga	tgggtgggga	4560
gcaaatcctc	tgcattcctg	atgaccaatg	ggatgagggt	actttttttt	ttttccccct	4620
tgaggattgc	ggaaaaccag	gaaaagggat	ctatgatttt	tttttccaaa	acaatttctt	4680
ttttaaaaag	actattttat	atgattcaca	tgctaaagcc	aggatttgtt	tgggttgaat	4740
atattttaag	tatcagagggt	ctatttttac	ctactgtgtc	ttggaatcta	gccgatggaa	4800
aatacctaag	tgtggatgat	galtgcgcag	ggagggggtac	gtggcacctc	ttccgaatgg	4860
gttttctatt	tgaacatgtg	ccttttctga	attatgcttc	cacaggcaaa	actcagtaga	4920
gatctatatt	tttgtactga	atctcataat	tgggaatatac	ggaataattta	aacagtagct	4980
tagcatcaga	ggttttgcttc	ctcagtaaca	tttctgttct	catttgatca	ggggaggcct	5040
ctttgccccg	gccccgcttc	ccctgcccc	gtgtgatttg	tgtccattt	tttcttccct	5100
tttccctccc	agttttc					5117

<210> 160

<211> 1337

<212> PRT

<213> Homo sapiens

<400> 160

```

Met Lys Pro Ala Ala Arg Glu Ala Arg Leu Pro Pro Arg Ser Pro Gly
 1           5           10           15
Leu Arg Trp Ala Leu Pro Leu Leu Leu Leu Leu Leu Arg Leu Gly Gln
          20           25           30
Ile Leu Cys Ala Gly Gly Thr Pro Ser Pro Ile Pro Asp Pro Ser Val
          35           40           45
Ala Thr Val Ala Thr Gly Glu Asn Gly Ile Thr Gln Ile Ser Ser Thr
          50           55           60
Ala Glu Ser Phe His Lys Gln Asn Gly Thr Gly Thr Pro Gln Val Glu
65          70          75          80
Thr Asn Thr Ser Glu Asp Gly Glu Ser Ser Gly Ala Asn Asp Ser Leu
          85          90          95
Arg Thr Pro Glu Gln Gly Ser Asn Gly Thr Asp Gly Ala Ser Gln Lys
          100         105         110
Thr Pro Ser Ser Thr Gly Pro Ser Pro Val Phe Asp Ile Lys Ala Val
          115         120         125
Ser Ile Ser Pro Thr Asn Val Ile Leu Thr Trp Lys Ser Asn Asp Thr
          130         135         140
Ala Ala Ser Glu Tyr Lys Tyr Val Val Lys His Lys Met Glu Asn Glu
145         150         155         160
Lys Thr Ile Thr Val Val His Gln Pro Trp Cys Asn Ile Thr Gly Leu
          165         170         175
Arg Pro Ala Thr Ser Tyr Val Phe Ser Ile Thr Pro Gly Ile Gly Asn
          180         185         190
Glu Thr Trp Gly Asp Pro Arg Val Ile Lys Val Ile Thr Glu Pro Ile
          195         200         205
Pro Val Ser Asp Leu Arg Val Ala His Gly Cys Glu Glu Gly Cys Ser
          210         215         220
Leu Ser Trp Ser Asn Gly Asn Gly Thr Ala Ser Cys Arg Val Leu Leu
225         230         235         240
Glu Ser Ile Gly Ser His Glu Glu Leu Thr Gln Asp Ser Arg Leu Gln
          245         250         255
Val Asn Ile Ser Asp Leu Lys Pro Gly Val Gln Tyr Asn Ile Asn Pro
          260         265         270
Tyr Leu Leu Gln Ser Asn Lys Thr Lys Gly Asp Pro Leu Ala Gln Lys
          275         280         285
Val Ala Trp Met Pro Ala Ile Gln Arg Glu Ala Gly Gln Gly Ala Pro
          290         295         300
Pro Pro Leu Cys Met Met Ser Pro Phe Val Gly Pro Val Asp Pro Ser
305         310         315         320
Ser Gly Gln Gln Ser Arg Asp Thr Glu Val Leu Leu Val Gly Leu Glu
          325         330         335
Pro Gly Thr Arg Tyr Asn Ala Thr Val Tyr Ser Gln Ala Ala Asn Gly
          340         345         350
Thr Glu Gly Gln Pro Gln Ala Ile Glu Phe Arg Thr Asn Ala Ile Gln
          355         360         365
Val Phe Asp Val Thr Ala Val Asn Ile Ser Ala Thr Ser Leu Thr Leu
          370         375         380
Ile Trp Lys Val Ser Asp Asn Glu Ser Ser Ser Asn Tyr Thr Tyr Lys
385         390         395         400
Ile His Val Ala Gly Glu Thr Asp Ser Ser Asn Leu Asn Val Ser Glu
          405         410         415
Pro Arg Ala Val Ile Pro Gly Leu Arg Ser Ser Thr Phe Tyr Asn Ile
          420         425         430

```

Thr Val Cys Pro Val Leu Gly Asp Ile Glu Gly Thr Pro Gly Phe Leu
 435 440 445
 Gln Val His Thr Pro Pro Val Pro Val Ser Asp Phe Arg Val Thr Val
 450 455 460
 Val Ser Thr Thr Glu Ile Gly Leu Ala Trp Ser Ser His Asp Ala Glu
 465 470 475 480
 Ser Phe Gln Met His Ile Thr Gln Glu Gly Ala Gly Asn Ser Arg Val
 485 490 495
 Glu Ile Thr Thr Asn Gln Ser Ile Ile Gly Gly Leu Phe Pro Gly
 500 505 510
 Thr Lys Tyr Cys Phe Glu Ile Val Pro Lys Gly Pro Asn Gly Thr Glu
 515 520 525
 Gly Ala Ser Arg Thr Val Cys Asn Arg Thr Val Pro Ser Ala Val Phe
 530 535 540
 Asp Ile His Val Val Tyr Val Thr Thr Thr Glu Met Trp Leu Asp Trp
 545 550 555 560
 Lys Ser Pro Asp Gly Ala Ser Glu Tyr Val Tyr His Leu Val Ile Glu
 565 570 575
 Ser Lys His Gly Ser Asn His Thr Ser Thr Tyr Asp Lys Ala Ile Thr
 580 585 590
 Leu Gln Gly Leu Ile Pro Gly Thr Leu Tyr Asn Ile Thr Ile Ser Pro
 595 600 605
 Glu Val Asp His Val Trp Gly Asp Pro Asn Ser Thr Ala Gln Tyr Thr
 610 615 620
 Arg Pro Ser Asn Val Ser Asn Ile Asp Val Ser Thr Asn Thr Thr Ala
 625 630 635 640
 Ala Thr Leu Ser Trp Gln Asn Phe Asp Asp Ala Ser Pro Thr Tyr Ser
 645 650 655
 Tyr Cys Leu Leu Ile Glu Lys Ala Gly Asn Ser Ser Asn Ala Thr Gln
 660 665 670
 Val Val Thr Asp Ile Gly Ile Thr Asp Ala Thr Val Thr Glu Leu Ile
 675 680 685
 Pro Gly Ser Ser Tyr Thr Val Glu Leu Phe Ala Gln Val Gly Asp Gly
 690 695 700
 Ile Lys Ser Leu Glu Pro Gly Arg Lys Ser Phe Cys Thr Asp Pro Ala
 705 710 715 720
 Ser Met Ala Ser Phe Asp Cys Glu Val Val Pro Lys Glu Pro Ala Leu
 725 730 735
 Val Leu Lys Trp Thr Cys Pro Pro Gly Ala Asn Ala Gly Phe Glu Leu
 740 745 750
 Glu Val Ser Ser Gly Ala Trp Asn Asn Ala Thr His Leu Glu Ser Cys
 755 760 765
 Ser Ser Glu Asn Gly Thr Glu Tyr Arg Thr Glu Val Thr Tyr Leu Asn
 770 775 780
 Phe Ser Thr Ser Tyr Asn Ile Ser Ile Thr Thr Val Ser Cys Gly Lys
 785 790 795 800
 Met Ala Ala Pro Thr Arg Asn Thr Cys Thr Thr Gly Ile Thr Asp Pro
 805 810 815
 Pro Pro Pro Asp Gly Ser Pro Asn Ile Thr Ser Val Ser His Asn Ser
 820 825 830
 Val Lys Val Lys Phe Ser Gly Phe Glu Ala Ser His Gly Pro Ile Lys
 835 840 845
 Ala Tyr Ala Val Ile Leu Thr Thr Gly Glu Ala Gly His Pro Ser Ala
 850 855 860
 Asp Val Leu Lys Tyr Thr Tyr Asp Asp Phe Lys Lys Gly Ala Ser Asp
 865 870 875 880
 Thr Tyr Val Thr Tyr Leu Ile Arg Thr Glu Glu Lys Gly Arg Ser Gln
 885 890 895

Ser Leu Ser Glu Val Leu Lys Tyr Glu Ile Asp Val Gly Asn Glu Ser
 900 905 910
 Thr Thr Leu Gly Tyr Tyr Asn Gly Lys Leu Glu Pro Leu Gly Ser Tyr
 915 920 925
 Arg Ala Cys Val Ala Gly Phe Thr Asn Ile Thr Phe His Pro Gln Asn
 930 935 940
 Lys Gly Leu Ile Asp Gly Ala Glu Ser Tyr Val Ser Phe Ser Arg Tyr
 945 950 955 960
 Ser Asp Ala Val Ser Leu Pro Gln Asp Pro Gly Val Ile Cys Gly Ala
 965 970 975
 Val Phe Gly Cys Ile Phe Gly Ala Leu Val Ile Val Thr Val Gly Gly
 980 985 990
 Phe Ile Phe Trp Arg Lys Lys Arg Lys Asp Ala Lys Asn Asn Glu Val
 995 1000 1005
 Ser Phe Ser Gln Ile Lys Pro Lys Lys Ser Lys Leu Ile Arg Val Glu
 1010 1015 1020
 Asn Phe Glu Ala Tyr Phe Lys Lys Gln Gln Ala Asp Ser Asn Cys Gly
 1025 1030 1035 1040
 Phe Ala Glu Glu Tyr Glu Asp Leu Lys Leu Val Gly Ile Ser Gln Pro
 1045 1050 1055
 Lys Tyr Ala Ala Glu Leu Ala Glu Asn Arg Gly Lys Asn Arg Tyr Asn
 1060 1065 1070
 Asn Val Leu Pro Tyr Asp Ile Ser Arg Val Lys Leu Ser Val Gln Thr
 1075 1080 1085
 His Ser Thr Asp Asp Tyr Ile Asn Ala Asn Tyr Met Pro Gly Tyr His
 1090 1095 1100
 Ser Lys Lys Asp Phe Ile Ala Thr Gln Gly Pro Leu Pro Asn Thr Leu
 1105 1110 1115 1120
 Lys Asp Phe Trp Arg Met Val Trp Glu Lys Asn Val Tyr Ala Ile Ile
 1125 1130 1135
 Met Leu Thr Lys Cys Val Glu Gln Gly Arg Thr Lys Cys Glu Glu Tyr
 1140 1145 1150
 Trp Pro Ser Lys Gln Ala Gln Asp Tyr Gly Asp Ile Thr Val Ala Met
 1155 1160 1165
 Thr Ser Glu Ile Val Leu Pro Glu Trp Thr Ile Arg Asp Phe Thr Val
 1170 1175 1180
 Lys Asn Ile Gln Thr Ser Glu Ser His Pro Leu Arg Gln Phe His Phe
 1185 1190 1195 1200
 Thr Ser Trp Pro Asp His Gly Val Pro Asp Thr Thr Asp Leu Leu Ile
 1205 1210 1215
 Asn Phe Arg Tyr Leu Val Arg Asp Tyr Met Lys Gln Ser Pro Pro Glu
 1220 1225 1230
 Ser Pro Ile Leu Val His Cys Ser Ala Gly Val Gly Arg Thr Gly Thr
 1235 1240 1245
 Phe Ile Ala Ile Asp Arg Leu Ile Tyr Gln Ile Glu Asn Glu Asn Thr
 1250 1255 1260
 Val Asp Val Tyr Gly Ile Val Tyr Asp Leu Arg Met His Arg Pro Leu
 1265 1270 1275 1280
 Met Val Gln Thr Glu Asp Gln Tyr Val Phe Leu Asn Gln Cys Val Leu
 1285 1290 1295
 Asp Ile Val Arg Ser Gln Lys Asp Ser Lys Val Asp Leu Ile Tyr Gln
 1300 1305 1310
 Asn Thr Thr Ala Met Thr Ile Tyr Glu Asn Leu Ala Pro Val Thr Thr
 1315 1320 1325
 Phe Gly Lys Thr Asn Gly Tyr Ile Ala
 1330 1335

<210> 161
 <211> 3984
 <212> DNA
 <213> Homo sapiens

<400> 161

```

ctgcaggtta ttcagcgata gttatgacct cccggttacg tgcgttgggt ggaagaatta 60
ataatatacg cacctcggag ttacccaaag agaaaactcg atcagaagtc atttgcagca 120
tccactttttt agatggcgtg gtacagacct ttaaagttac taaacaagac actggccagg 180
ttcttctgga tatggtgcac aaccacctgg gtgtgactga aaaggaatat tttggtttac 240
agcatgatga cgactccgtg gactctccta gatggctgga agcaagcaaa cccatcagga 300
agcagttaaa aggaggtttc ccctgtaccc tgcatttttc agtaagattt tttataacctg 360
atcccaacac actgcagcaa gaacaaacca ggcacttgta tttcttacia ctgaagatgg 420
atatttgcca aggaaggtta acctgccctc ttaactcagc agtggttcta gcgtcctatg 480
ccgtacaatc tcatttttga gactataatt cttccataca tcatccaggc tatctttccg 540
atagtcactt tatacccgat caaaatgagg accttttaac aaaagtcgaa tctctgcatg 600
agcagcacag tgggctaata caatcagaag cagaatcctg ctatatcaac atagcgcgga 660
ccctcgactt ctatggagta gaactgcaca gtggtaggga tctgcacaat ttagacctaa 720
tgattggaat tgcttccgag ggtgttgctg tgtaccgaaa atacatttgc acaagtttct 780
atccttgggt gaacattctc aaaatttctt tcaaaaggaa aaagttcttc atacatcagc 840
gacagaaaca ggctgaatcc agggaaacata ttgtggcctt caacatgctg aattaccgat 900
cttgcaaaaa cttgtggaat tctgtgttg agcaccatac gttctttcag gcaaagaagc 960
tactacctca ggaaaagaat gttctgtctc agtactggac tatgggctct cggaacacca 1020
aaaagtcggt aaataaccaa tattgcaaaa aggtgattgg cgggatgggtg tggaaaccag 1080
ccatgcggag atccttatca gtggagcact tagaaaccaa gagtctgcct tctcgttccc 1140
ctcccattac tcccaactgg cgaagtcctc ggctccggca cgaaatccga aagccacgct 1200
actcttctgc agataacctt gcaaataaaa tgacctacat caccgaaacg gaagatgtat 1260
tttacacgta caagggctct ctggccctct aagacagcga ttctgaagtt tctcagaacc 1320
gaagcccgca ccaagagagt ttatccgaga acaatccggc acaaagctac ctgaccaga 1380
agtcateccag ttctgtgtct ccatcttcaa atgctccagg ctctgtctca cctgacggcg 1440
ttgatcagca gctcttagat gacttccaca ggggtgacaa agggggctcc accgaggacg 1500
ccagccagta ctactgtgac aagaatgata atgggtgacag ctacttagtc ttgatccgta 1560
tcacaccaga tgaagatgga aaatttggat ttaactttaa gggaggagtg gatcaaaaga 1620
tgctctttgt ggtatcaagg ataaacccag agtcacctgc ggacacctgc attcctaagc 1680
tgaacgaagg ggtatcaaat gtgttaatca atggccggga catctcagaa cacacgcatg 1740
accaagtggg gatgttcate aaagccagcc gggagtccca ctacacggag ctggccctgg 1800
tgatcaggag gagagctgtc cgtcatttgg ctgacttcaa gtctgaagat gaactgaacc 1860
agcttttccc cgaagccatt ttcccatatg gtccggaggg tggggacact ttggagggat 1920
ccatggcaca gctaaagaag ggctcgaaa gcgggacggt gctgatccag tttgagcaac 1980
tctacagaaa aaagccagg ttggccatca cgtttgcaaa gctgcctcaa aatttggaca 2040
aaaaccgata taaagatgtg ctgccttatg acaccaccg ggtattattg cagggaatg 2100
aagattatat taatgcaagt tacgtgaaca tggaaattcc tgctgctaac cttgtgaaca 2160
agtacatcgc cactcagggg cccctgccgc atacctgtgc acagttttgg cagggtgtct 2220
gggatcagaa gttgtcactc attgtcatgt tgacgactct cacagaacga gggcggacca 2280
aatgtcacca gtactggcca gatccccccg acgtcatgaa ccacggcggc tttcacatcc 2340
agtgtcagtc agaggactgc accatcgctt atgtgtccc agaaaatgctg gtcacaaaca 2400
cccagaccgg ggaagaacac acagtgcac atctccagta cgtcgcatgg cctgaccacg 2460
gtatacccca tgactcctcc gactttctgg aatttgtaaa ctatgtgagg tctctgagag 2520
tggacagcga gctgtccta gttcactgca gtgtggaat aggtcgaacc ggtgtgttgg 2580
tactatgga aacagccatg tgccctaact agaggaacct gccatttac ccactggata 2640
ttgtccgaaa aatgcgagac cagcgcgcga tgatgggtga gacatcaagc cagtacaagt 2700
ttgtgtgtga agcgattctt cgtgtgtatg aagaagggtt ctttcccaag ggcattcctc 2760
gttaagacaa ctgtgaaaaa gticatttct ctttcccaag ggcattcctc ttgaaagagg 2820
aggacagacc tctctggaag cagcaagagg aaccagtagc tgtgggaaag gaatgggcac 2880
ctctgaaccc aggcacttta aacttctata gaaaagatat cgtgtacata ggaactgggtg 2940
tagataagca tgcaattatg gcatcattta ggctgtatt tctatggaaa gatacaaaaa 3000
ggatctcagt ttggggcctg tctaatgcc ttcttcccta acatcaccac acacaccct 3060
gtcggcatcc tggagcaatt gagaccggac acccacagag ctgttgtctt cccagcaaca 3120

```

```

agatgggtgtg gttatcttgg gtcatttggg tgttttgttt gtttctgtgt gtcagactgt 3180
aagggctgag ctttctgtgc ttctaggtgg agctggaaca attcagattc acccgccctg 3240
atgctaagga aaccctgacg tatgtactag atggcagggc actgggggtc aggctgaagg 3300
ctgagcaaca cctctctgcc ctccctccct ttgtcccatc tcccagcgac ttccaatatt 3360
catgtttctg agaattgtgt cctctctcag ttccctcttg gtgcctaacc tggattagta 3420
atgtgcattc aggtgaattt tcagctgagg ctctgagaac tggactctc agtgtgttct 3480
ggtcattctt tggcttagtt gtagaagcag gtgtgtctct tgcctctgct tgcctcctac 3540
tgcacactca gcaccagga ctggaatcac cgactactga atctcctaca tgtattgctg 3600
ctacttcaag ctccctccact tgaaacctta tgattttcca aggggagatg ggacagtgtc 3660
atctaaatat tccgaatgtt tggccttctg agaaaagagc ttctagtaat tgaaccatgg 3720
gtttcccagc ttctggaggg ttggccgtgg gctgtgtaca tgtgtgtgcc caggggtgag 3780
tgtttctcag gattcctaac gattcaaatt accgttgagt atatataaag aatcgagtcg 3840
gaagaacaaa tgtgtgcatt caccctcagt cacaatggtc tccattgcat ttcaaaggag 3900
aggatcagac tatctgaata taaacacaat ctgatgttaa tttattctaa gaacaccatc 3960
tgatttcatt ttgattgtcc taaa 3984

```

<210> 162

<211> 913

<212> PRT

<213> Homo sapiens

<400> 162

```

Met Thr Ser Arg Leu Arg Ala Leu Gly Gly Arg Ile Asn Asn Ile Arg
 1          5          10          15
Thr Ser Glu Leu Pro Lys Glu Lys Thr Arg Ser Glu Val Ile Cys Ser
 20          25          30
Ile His Phe Leu Asp Gly Val Val Gln Thr Phe Lys Val Thr Lys Gln
 35          40          45
Asp Thr Gly Gln Val Leu Leu Asp Met Val His Asn His Leu Gly Val
 50          55          60
Thr Glu Lys Glu Tyr Phe Gly Leu Gln His Asp Asp Ser Val Asp
 65          70          75          80
Ser Pro Arg Trp Leu Glu Ala Ser Lys Pro Ile Arg Lys Gln Leu Lys
 85          90          95
Gly Gly Phe Pro Cys Thr Leu His Phe Arg Val Arg Phe Phe Ile Pro
100          105          110
Asp Pro Asn Thr Leu Gln Gln Glu Gln Thr Arg His Leu Tyr Phe Leu
115          120          125
Gln Leu Lys Met Asp Ile Cys Glu Gly Arg Leu Thr Cys Pro Leu Asn
130          135          140
Ser Ala Val Val Leu Ala Ser Tyr Ala Val Gln Ser His Phe Gly Asp
145          150          155          160
Tyr Asn Ser Ser Ile His His Pro Gly Tyr Leu Ser Asp Ser His Phe
165          170          175
Ile Pro Asp Gln Asn Glu Asp Phe Leu Thr Lys Val Glu Ser Leu His
180          185          190
Glu Gln His Ser Gly Leu Lys Gln Ser Glu Ala Glu Ser Cys Tyr Ile
195          200          205
Asn Ile Ala Arg Thr Leu Asp Phe Tyr Gly Val Glu Leu His Ser Gly
210          215          220
Arg Asp Leu His Asn Leu Asp Leu Met Ile Gly Ile Ala Ser Ala Gly
225          230          235          240
Val Ala Val Tyr Arg Lys Tyr Ile Cys Thr Ser Phe Tyr Pro Trp Val
245          250          255
Asn Ile Leu Lys Ile Ser Phe Lys Arg Lys Lys Phe Phe Ile His Gln
260          265          270
Arg Gln Lys Gln Ala Glu Ser Arg Glu His Ile Val Ala Phe Asn Met
275          280          285

```

Leu	Asn	Tyr	Arg	Ser	Cys	Lys	Asn	Leu	Trp	Lys	Ser	Cys	Val	Glu	His
290						295					300				
His	Thr	Phe	Phe	Gln	Ala	Lys	Lys	Leu	Leu	Pro	Gln	Glu	Lys	Asn	Val
305				310						315					320
Leu	Ser	Gln	Tyr	Trp	Thr	Met	Gly	Ser	Arg	Asn	Thr	Lys	Lys	Ser	Val
			325						330						335
Asn	Asn	Gln	Tyr	Cys	Lys	Lys	Val	Ile	Gly	Gly	Met	Val	Trp	Asn	Pro
		340						345					350		
Ala	Met	Arg	Arg	Ser	Leu	Ser	Val	Glu	His	Leu	Glu	Thr	Lys	Ser	Leu
	355						360					365			
Pro	Ser	Arg	Ser	Pro	Pro	Ile	Thr	Pro	Asn	Trp	Arg	Ser	Pro	Arg	Leu
	370					375					380				
Arg	His	Glu	Ile	Arg	Lys	Pro	Arg	His	Ser	Ser	Ala	Asp	Asn	Leu	Ala
385					390					395					400
Asn	Glu	Met	Thr	Tyr	Ile	Thr	Glu	Thr	Glu	Asp	Val	Phe	Tyr	Thr	Tyr
			405						410						415
Lys	Gly	Ser	Leu	Ala	Pro	Gln	Asp	Ser	Asp	Ser	Glu	Val	Ser	Gln	Asn
			420					425					430		
Arg	Ser	Pro	His	Gln	Glu	Ser	Leu	Ser	Glu	Asn	Asn	Pro	Ala	Gln	Ser
	435						440					445			
Tyr	Leu	Thr	Gln	Lys	Ser	Ser	Ser	Ser	Val	Ser	Pro	Ser	Ser	Asn	Ala
	450					455					460				
Pro	Gly	Ser	Cys	Ser	Pro	Asp	Gly	Val	Asp	Gln	Gln	Leu	Leu	Asp	Asp
465					470					475					480
Phe	His	Arg	Val	Thr	Lys	Gly	Gly	Ser	Thr	Glu	Asp	Ala	Ser	Gln	Tyr
			485						490						495
Tyr	Cys	Asp	Lys	Asn	Asp	Asn	Gly	Asp	Ser	Tyr	Leu	Val	Leu	Ile	Arg
	500							505					510		
Ile	Thr	Pro	Asp	Glu	Asp	Gly	Lys	Phe	Gly	Phe	Asn	Leu	Lys	Gly	Gly
	515						520					525			
Val	Asp	Gln	Lys	Met	Pro	Leu	Val	Val	Ser	Arg	Ile	Asn	Pro	Glu	Ser
	530					535						540			
Pro	Ala	Asp	Thr	Cys	Ile	Pro	Lys	Leu	Asn	Glu	Gly	Asp	Gln	Ile	Val
545					550					555					560
Leu	Ile	Asn	Gly	Arg	Asp	Ile	Ser	Glu	His	Thr	His	Asp	Gln	Val	Val
			565						570						575
Met	Phe	Ile	Lys	Ala	Ser	Arg	Glu	Ser	His	Ser	Arg	Glu	Leu	Ala	Leu
		580						585					590		
Val	Ile	Arg	Arg	Arg	Ala	Val	Arg	Ser	Phe	Ala	Asp	Phe	Lys	Ser	Glu
	595						600					605			
Asp	Glu	Leu	Asn	Gln	Leu	Phe	Pro	Glu	Ala	Ile	Phe	Pro	Met	Cys	Pro
	610					615					620				
Glu	Gly	Gly	Asp	Thr	Leu	Glu	Gly	Ser	Met	Ala	Gln	Leu	Lys	Lys	Gly
625					630					635					640
Leu	Glu	Ser	Gly	Thr	Val	Leu	Ile	Gln	Phe	Glu	Gln	Leu	Tyr	Arg	Lys
			645						650						655
Lys	Pro	Gly	Leu	Ala	Ile	Thr	Phe	Ala	Lys	Leu	Pro	Gln	Asn	Leu	Asp
		660						665					670		
Lys	Asn	Arg	Tyr	Lys	Asp	Val	Leu	Pro	Tyr	Asp	Thr	Thr	Arg	Val	Leu
	675						680					685			
Leu	Gln	Gly	Asn	Glu	Asp	Tyr	Ile	Asn	Ala	Ser	Tyr	Val	Asn	Met	Glu
	690					695					700				
Ile	Pro	Ala	Ala	Asn	Leu	Val	Asn	Lys	Tyr	Ile	Ala	Thr	Gln	Gly	Pro
705					710					715					720
Leu	Pro	His	Thr	Cys	Ala	Gln	Phe	Trp	Gln	Val	Val	Trp	Asp	Gln	Lys
			725						730						735
Leu	Ser	Leu	Ile	Val	Met	Leu	Thr	Thr	Leu	Thr	Glu	Arg	Gly	Arg	Thr
			740						745						750

Lys Cys His Gln Tyr Trp Pro Asp Pro Pro Asp Val Met Asn His Gly
 755 760 765
 Gly Phe His Ile Gln Cys Gln Ser Glu Asp Cys Thr Ile Ala Tyr Val
 770 775 780
 Ser Arg Glu Met Leu Val Thr Asn Thr Gln Thr Gly Glu Glu His Thr
 785 790 795 800
 Val Thr His Leu Gln Tyr Val Ala Trp Pro Asp His Gly Ile Pro Asp
 805 810 815
 Asp Ser Ser Asp Phe Leu Glu Phe Val Asn Tyr Val Arg Ser Leu Arg
 820 825 830
 Val Asp Ser Glu Pro Val Leu Val His Cys Ser Ala Gly Ile Gly Arg
 835 840 845
 Thr Gly Val Leu Val Thr Met Glu Thr Ala Met Cys Leu Thr Glu Arg
 850 855 860
 Asn Leu Pro Ile Tyr Pro Leu Asp Ile Val Arg Lys Met Arg Asp Gln
 865 870 875 880
 Arg Ala Met Met Val Gln Thr Ser Ser Gln Tyr Lys Phe Val Cys Glu
 885 890 895
 Ala Ile Leu Arg Val Tyr Glu Glu Gly Leu Val Gln Met Leu Asp Pro
 900 905 910
 Ser

<210> 163
 <211> 2287
 <212> DNA
 <213> Homo sapien

<400> 163
 ggggggcctg agcctctccg ccggcgcagg ctctgctcgc gccagctcgc tcccgcagcc 60
 atgcccacca ccacgcagcg ggagttcgaa gaggttggata ctacgcgtcg ctggcagccg 120
 ctgtacttgg aaattcgaaa tgagtcocat gactatcctc atagagtggc caagtttcca 180
 gaaaacagaa atcgaaacag atacagagat gtaagcccat atgatcacag tcgtgtttaa 240
 ctgcaaaatg ctgagaatga ttatattaat gccagtttag ttgacataga agaggcacaa 300
 aggagttaca tcttaacaca gggtcactt cctaacacat gctgccattt ctggccttatg 360
 gtttggcagc agaagaccaa agcagttgtc atgctgaacc gcattgtgga gaaagaatcg 420
 gttaaattgt cacagtactg gccaacagat gaccaagaga tgctgtttta agaaacagga 480
 ttcaagtgtg agctcttgtc agaagatgtg aagtcgtatt atacagtaca tctactacaa 540
 ttagaaaata tcaatagtgg tgaaaccaga acaatatctc actttcatta tactacctgg 600
 ccagattttg gagtccctga atcaccagct tcattttctc atttcttgtt taaagtgaga 660
 gaatctggct ccttgaaccc tgaccatggg cctgcggtga tccactgtag tgcaggcatt 720
 gggcgcctct gcaccttctc tctggtagac acttgtcttg ttttgatgga aaaaggagat 780
 gatattaaca taaaacaagt gttactgaac atgagaaaat accgaatggg tcttattcag 840
 accccagatc aactgagatt ctcatatcat gctataatag aaggagcaaa atgtataaag 900
 ggagattcta gtatacagaa acgatggaaa gaactttcta aggaagactt atctcctgcc 960
 tttgatcatt caccaaaca aataatgact gaaaaatata atgggaacag aataggtcta 1020
 gaagaagaaa aactgacagg tgaccgatgt acaggacttt cctctaaaat gcaagatata 1080
 atggaggaga acagtgcagg tgctctacgg aaacgtatc gagaggacag aaaggccacc 1140
 acagctcaga aggtgcagca gatgaaacag aggtctaaatg agaatgaacg aaaaagaaaa 1200
 aggtggttat attggcaacc tattctcact aagatggggg ttatgtcagt catttttggtt 1260
 ggcgcttttg ttggctggag actgtttttt cagcaaaatg cctataaac aattaatttt 1320
 gccagcaag cttctgcact agtaactgac agtgctacat taatcatagg ggtttgtctg 1380
 cagcaaacgc ctcatatccc aaaaacgggt cagtagaata gacatcaacc agataagtga 1440
 tatttacagt cacaagccca acatctcagg actcttgact gcaggttcct ctgaacccca 1500
 aactgtaaat ggctgtctaa aataaagaca ttcatgtttg ttaaaaactg gtaaattttg 1560
 caactgtatt catacatgtc aaacacagta ttacacctga ccaacattga gatatccttt 1620
 atcacaggat ttgttttttg aggcctatctg gattttaacc tgcacttgat ataagcaata 1680

```

aatattgtgg ttttatctac gttattggaa agaaaatgac atttaaataa tgtgtgtaat 1740
gtataatgta ctattgacat gggcatcaac actttttattc ttaagcattt cagggtaaat 1800
atatatttata agtatctatt taatcttttg tagttaactg tacttttttaa gagctcaatt 1860
tgaaaaatct gttactaaaa aaaaaaattg tatgtcgatt gaattgtact ggatacattt 1920
tccatttttc taaaaagaag ttgatatga gcagttagaa gttggaataa gcaatttcta 1980
ctatatattg cttttctttt atgtttttaca gttttcccca ttttaaaaag aaaagcaaac 2040
aaagaaacaa aagtttttcc taaaaatattc tttgaaggaa aattctcctt actgggatag 2100
tcaggtaaac agttgggtcaa gactttgtaa agaaattggg ttctgtaaat cccattattg 2160
atatgtttat ttttcatgaa aattttcaatg tagttggggg agattatgat ttaggaagca 2220
aaagtaagaa gcagcatttt atgattcata atttcagttt actagactga agttttgaag 2280
taaacc 2287

```

<210> 164

<211> 415

<212> PRT

<213> Homo sapiens

<400> 164

```

Met Pro Thr Thr Ile Glu Arg Glu Phe Glu Glu Leu Asp Thr Gln Arg
1      5      10      15
Arg Trp Gln Pro Leu Tyr Leu Glu Ile Arg Asn Glu Ser His Asp Tyr
      20      25      30
Pro His Arg Val Ala Lys Phe Pro Glu Asn Arg Asn Arg Asn Arg Tyr
      35      40      45
Arg Asp Val Ser Pro Tyr Asp His Ser Arg Val Lys Leu Gln Asn Ala
      50      55      60
Glu Asn Asp Tyr Ile Asn Ala Ser Leu Val Asp Ile Glu Glu Ala Gln
65      70      75      80
Arg Ser Tyr Ile Leu Thr Gln Gly Pro Leu Pro Asn Thr Cys Cys His
      85      90      95
Phe Trp Leu Met Val Trp Gln Gln Lys Thr Lys Ala Val Val Met Leu
      100     105     110
Asn Arg Ile Val Glu Lys Glu Ser Val Lys Cys Ala Gln Tyr Trp Pro
      115     120     125
Thr Asp Asp Gln Glu Met Leu Phe Lys Glu Thr Gly Phe Ser Val Lys
130     135     140
Leu Leu Ser Glu Asp Val Lys Ser Tyr Tyr Thr Val His Leu Leu Gln
145     150     155     160
Leu Glu Asn Ile Asn Ser Gly Glu Thr Arg Thr Ile Ser His Phe His
      165     170     175
Tyr Thr Thr Trp Pro Asp Phe Gly Val Pro Glu Ser Pro Ala Ser Phe
      180     185     190
Leu Asn Phe Leu Phe Lys Val Arg Glu Ser Gly Ser Leu Asn Pro Asp
      195     200     205
His Gly Pro Ala Val Ile His Cys Ser Ala Gly Ile Gly Arg Ser Gly
210     215     220
Thr Phe Ser Leu Val Asp Thr Cys Leu Val Leu Met Glu Lys Gly Asp
225     230     235     240
Asp Ile Asn Ile Lys Gln Val Leu Leu Asn Met Arg Lys Tyr Arg Met
      245     250     255
Gly Leu Ile Gln Thr Pro Asp Gln Leu Arg Phe Ser Tyr Met Ala Ile
      260     265     270
Ile Glu Gly Ala Lys Cys Ile Lys Gly Asp Ser Ser Ile Gln Lys Arg
      275     280     285
Trp Lys Glu Leu Ser Lys Glu Asp Leu Ser Pro Ala Phe Asp His Ser
290     295     300
Pro Asn Lys Ile Met Thr Glu Lys Tyr Asn Gly Asn Arg Ile Gly Leu
305     310     315     320

```

Glu	Glu	Glu	Lys	Leu	Thr	Gly	Asp	Arg	Cys	Thr	Gly	Leu	Ser	Ser	Lys
				325					330					335	
Met	Gln	Asp	Thr	Met	Glu	Glu	Asn	Ser	Glu	Ser	Ala	Leu	Arg	Lys	Arg
			340					345					350		
Ile	Arg	Glu	Asp	Arg	Lys	Ala	Thr	Thr	Ala	Gln	Lys	Val	Gln	Gln	Met
		355				360					365				
Lys	Gln	Arg	Leu	Asn	Glu	Asn	Glu	Arg	Lys	Arg	Lys	Arg	Trp	Leu	Tyr
	370				375					380					
Trp	Gln	Pro	Ile	Leu	Thr	Lys	Met	Gly	Phe	Met	Ser	Val	Ile	Leu	Val
385				390					395					400	
Gly	Ala	Phe	Val	Gly	Trp	Arg	Leu	Phe	Phe	Gln	Gln	Asn	Ala	Leu	
			405					410						415	

<210> 165

<211> 2477

<212> DNA

<213> Homo sapiens

<400> 165

```

gctcggggcgc cgagtctgcg cgctgacgtc cgacgctcca ggtactttcc ccacggccga 60
cagggccttgg cgtggggggcg gggcgcggcg cgcagcgcgc atgcgcgcga ggcgcagcgc 120
tctccccgga tcgtgcgggg cctgagcctc tccgcggcg caggctctgc tcgcgccagc 180
tcgctcccg cgcctatgcc accaccatcg agcgggagtt cgaagagttg gatactcagc 240
gtcgtcggca gccgctgtac ttggaaattc gaaatgagtc ccatgactat cctcatagag 300
tggccaagtt tccagaaaac agaaatcgaa acagatacag agatgtaagc ccatatgac 360
acagtcgtgt taaactgcaa aatgctgaga atgattatat taatgccagt ttagttgaca 420
tagaagaggc acaaaggagt tacatcttaa cacagggtcc acttcctaac acatgctgcc 480
atctctggct tatggtttgg cagcagaaga ccaaagcagt tgtcatgctg aaccgcattg 540
tggagaaaaga atcggttaaa tgtgcacagt actggccaac agatgacca gagatgctgt 600
ttaaagaaac aggattcagt gtgaagctct tgtcagaaga tgtgaagtcg tattatacag 660
tacatctact acaattagaa aatatcaata gtggtgaaac cagaacaata tctcactttc 720
attatactac ctggccagat tttggagtc cagaatcacc agcttcattt ctcaatttct 780
tgtttaaagt gagagaatct ggctccttga accctgacca tgggcctgcg gtgatccact 840
gtagtgcagg cattgggcgc tctggcacct tctctctggg agacacttgt cttgttttga 900
tggaaaaagg agatgatatt aacataaaac aagtgttact gaacatgaga aaataccgaa 960
tgggtcttat tcagacccca gatcaactga gattctcata catggctata atagaaggag 1020
caaatgtat aaaggagat tctagtatac agaaacgatg gaaagaactt tctaagggaag 1080
acttatctcc tgcctttgat cattcaccaa acaaaataat gactgaaaaa tacaatggga 1140
acagaatagg tctagaagaa gaaaaactga caggtgaccg atgtacagga ctttctctta 1200
aaatgcaaga tacaatggag gagaacagtg agagtgtctc acggaaacgt attcgagagg 1260
acagaaaggc caccacagct cagaagggtg agcagatgaa acagaggcta aatgagaatg 1320
aacgaaaaag aaaaagggtg ttatatgtgg aacctattct cactaagatg gggtttatgt 1380
cagtcatttt gggtggcgct tttgttggct ggagactgtt ttttcagcaa aatgccctat 1440
aaacaattaa ttttgcccag caagcttctg cactagtaac tgacagtgtc acattaatca 1500
taggggtttg tctgcagcaa acgcctcata tcccaaaaac ggtgcagtag aatagacatc 1560
aaccagataa gtgatattta cagtcacaag cccaacatct caggactctt gactgcaggt 1620
tctctgaac cccaaactgt aaatggctgt ctaaaataaa gacattcatg tttgttaaaa 1680
actggtaaat tttgcaactg tattcatata tgtcaaacac agtatttcac ctgaccaaca 1740
ttgagataac ctttatcaca ggatttgggt ttggaggcta tctggatttt aacctgcact 1800
tgatataagc aataaatatt gtggttttat ctacgttatt ggaaagaaaa tgacatttaa 1860
ataatgtgtg taatgtataa tgtactattg acatgggcat caacactttt attcttaagc 1920
atctcagggg aaatatattt tataagttat tatttaatct tttgtagtta actgtacttt 1980
ttaagagctc aatttgaaaa atctgttact aaaaaaaaaa attgtatgtc gattgaattg 2040
tactggatac attttccatt tttctaaaaa gaagtttgat atgagcagtt agaagttgga 2100
ataagcaatt tctactatat attgcatttc ttttatgttt tacagttttc cccattttta 2160
aaagaaaagc aaacaaagaa acaaaagttt ttcttaaaaa tatctttgaa ggaaaattct 2220
ccttactggg atagtcaggt aaacagttgg tcaagacttt gtaaagaaat tggtttctgt 2280

```

```

aaatcccatt attgatatgt ttattttttca tgaaaatttc aatgtagttg gggtagatta 2340
tgatttagga agcaaaagta agaagcagca ttttatgatt cataatttca gtttactaga 2400
ctgaagtttt gaagtaaaca cttttcagtt tcttttact tcaataaata gtatgattat 2460
atgcaaacct taaaaaa 2477

```

<210> 166
 <211> 415
 <212> PRT
 <213> Homo sapiens

<400> 166

Met	Pro	Thr	Thr	Ile	Glu	Arg	Glu	Phe	Glu	Glu	Leu	Asp	Thr	Gln	Arg
1				5				10						15	
Arg	Trp	Gln	Pro	Leu	Tyr	Leu	Glu	Ile	Arg	Asn	Glu	Ser	His	Asp	Tyr
			20					25					30		
Pro	His	Arg	Val	Ala	Lys	Phe	Pro	Glu	Asn	Arg	Asn	Arg	Asn	Arg	Tyr
			35					40					45		
Arg	Asp	Val	Ser	Pro	Tyr	Asp	His	Ser	Arg	Val	Lys	Leu	Gln	Asn	Ala
	50					55					60				
Glu	Asn	Asp	Tyr	Ile	Asn	Ala	Ser	Leu	Val	Asp	Ile	Glu	Glu	Ala	Gln
65					70					75					80
Arg	Ser	Tyr	Ile	Leu	Thr	Gln	Gly	Pro	Leu	Pro	Asn	Thr	Cys	Cys	His
			85						90					95	
Phe	Trp	Leu	Met	Val	Trp	Gln	Gln	Lys	Thr	Lys	Ala	Val	Val	Met	Leu
			100					105					110		
Asn	Arg	Ile	Val	Glu	Lys	Glu	Ser	Val	Lys	Cys	Ala	Gln	Tyr	Trp	Pro
			115				120					125			
Thr	Asp	Asp	Gln	Glu	Met	Leu	Phe	Lys	Glu	Thr	Gly	Phe	Ser	Val	Lys
	130					135					140				
Leu	Leu	Ser	Glu	Asp	Val	Lys	Ser	Tyr	Tyr	Thr	Val	His	Leu	Leu	Gln
145					150					155					160
Leu	Glu	Asn	Ile	Asn	Ser	Gly	Glu	Thr	Arg	Thr	Ile	Ser	His	Phe	His
			165						170					175	
Tyr	Thr	Thr	Trp	Pro	Asp	Phe	Gly	Val	Pro	Glu	Ser	Pro	Ala	Ser	Phe
			180					185					190		
Leu	Asn	Phe	Leu	Phe	Lys	Val	Arg	Glu	Ser	Gly	Ser	Leu	Asn	Pro	Asp
			195				200					205			
His	Gly	Pro	Ala	Val	Ile	His	Cys	Ser	Ala	Gly	Ile	Gly	Arg	Ser	Gly
	210					215					220				
Thr	Phe	Ser	Leu	Val	Asp	Thr	Cys	Leu	Val	Leu	Met	Glu	Lys	Gly	Asp
225					230					235					240
Asp	Ile	Asn	Ile	Lys	Gln	Val	Leu	Leu	Asn	Met	Arg	Lys	Tyr	Arg	Met
			245						250					255	
Gly	Leu	Ile	Gln	Thr	Pro	Asp	Gln	Leu	Arg	Phe	Ser	Tyr	Met	Ala	Ile
			260					265					270		
Ile	Glu	Gly	Ala	Lys	Cys	Ile	Lys	Gly	Asp	Ser	Ser	Ile	Gln	Lys	Arg
			275				280					285			
Trp	Lys	Glu	Leu	Ser	Lys	Glu	Asp	Leu	Ser	Pro	Ala	Phe	Asp	His	Ser
	290					295					300				
Pro	Asn	Lys	Ile	Met	Thr	Glu	Lys	Tyr	Asn	Gly	Asn	Arg	Ile	Gly	Leu
305					310					315					320
Glu	Glu	Glu	Lys	Leu	Thr	Gly	Asp	Arg	Cys	Thr	Gly	Leu	Ser	Ser	Lys
			325						330					335	
Met	Gln	Asp	Thr	Met	Glu	Glu	Asn	Ser	Glu	Ser	Ala	Leu	Arg	Lys	Arg
			340					345					350		
Ile	Arg	Glu	Asp	Arg	Lys	Ala	Thr	Thr	Ala	Gln	Lys	Val	Gln	Gln	Met
			355				360					365			
Lys	Gln	Arg	Leu	Asn	Glu	Asn	Glu	Arg	Lys	Arg	Lys	Arg	Trp	Leu	Tyr

370		375		380
Trp Gln Pro Ile Leu Thr Lys Met Gly Phe Met Ser Val Ile Leu Val				
385		390		395
Gly Ala Phe Val Gly Trp Arg Leu Phe Phe Gln Gln Asn Ala Leu				400
	405		410	415

<210> 167
 <211> 1714
 <212> DNA
 <213> Homo sapiens

<400> 167

```

gctcgggcgc cgagtctgcg cgctgacgtc cgacgctcca ggtactttcc ccacggccga 60
cagggccttg cgtgggggcg gggcgcggcg cgcagcgcg atgcgccgca gcccagcgc 120
tctccccgga tcgtgcgggg cctgagcctc tccgcggcg caggctctgc tcgcgccagc 180
tcgctccgcg agccatgccc accaccatcg agcgggagtt cgaagagttg gatactcagc 240
gtcgctggca gccgctgtac ttggaaaattc gaaatgagtc ccatgactat cctcatagag 300
tggccaagtt tccagaaaac agaaatcgaa acagatacag agatgtaagc ccatatgac 360
acagtctgtg taaactgcaa aatgctgaga atgattatat taatgccagt ttagttgaca 420
tagaagaggc acaaaggagt tacatcttaa cacagggtcc acttcctaac acatgctgcc 480
atctctggct tatggtttgg cagcagaaga ccaaagcagt tgtcatgctg aaccgcattg 540
tggagaaaga atcggttaaa tgtgcacagt actggccaac agatgaccaa gagatgctgt 600
ttaaagaaac aggattcagt gtgaagctct tgtcagaaga tgtgaagtcg tattatacag 660
tacatctact acaattagaa aatatcaata gtggtgaaac cagaacaata tctcactttc 720
attatactac ctggccagat tttggagtc ctgaatcacc agcttcattt ctcaatttct 780
tgtttaaagt gagagaatct ggctccttga accctgacca tgggcctgcg gtgatccact 840
gtagtgcagg cattgggcgc tctggcacct tctctctgg agacacttgt cttgttttga 900
tggaaaaagg agatgatatt aacataaaac aagtgttact gaacatgaga aaataccgaa 960
tgggtcttat tcagacccca gatcaactga gattctcata catggctata atagaaggag 1020
caaatgtat aaagggagat tctagtatac agaaacgatg gaaagaactt tctaaggaag 1080
acttatctcc tgcctttgat cattcaccaa acaaaataat gactgaaaaa tacaatggga 1140
acagaatagg tctagaagaa gaaaaactga caggtgaccg atgtacagga ctttcctcta 1200
aaatgcaaga tacaatggag gagaacagtg agagtgcctc acggaaacgt attcgagagg 1260
acagaaaggc caccacagct cagaagggtgc agcagatgaa acagaggcta aatgagaatg 1320
aacgaaaaag aaaaaggcca agattgacag acacctaata ttcatgactt gagaatattc 1380
tgcagctata aattttgaac cattgatgtg caaagcaaga cctgaagccc actccggaaa 1440
ctaaagttag gctcgctaac cctctagatt gcctcacagt tgtttgttta caaagtaa 1500
tttacatcca ggggatgaag agcaccacc agcagaagac tttgcagaac ctttaattgg 1560
atgtgttaag tgtttttaat gagtgtatga aatgtagaaa gatgtacaag aaataaatta 1620
ggagagatta ctttgtattg tactgccatt cctactgtat ttttatactt tttggcagca 1680
ttaaatattt ttgttaaata aaaaaaaaaa aaaa 1714

```

<210> 168
 <211> 387
 <212> PRT
 <213> Homo sapiens

<400> 168

Met Pro Thr Thr Ile Glu Arg Glu Phe Glu Glu Leu Asp Thr Gln Arg	
1	5
Arg Trp Gln Pro Leu Tyr Leu Glu Ile Arg Asn Glu Ser His Asp Tyr	
	20
Pro His Arg Val Ala Lys Phe Pro Glu Asn Arg Asn Arg Asn Arg Tyr	
35	40
Arg Asp Val Ser Pro Tyr Asp His Ser Arg Val Lys Leu Gln Asn Ala	
50	55
Glu Asn Asp Tyr Ile Asn Ala Ser Leu Val Asp Ile Glu Glu Ala Gln	

65					70					75					80
Arg	Ser	Tyr	Ile	Leu	Thr	Gln	Gly	Pro	Leu	Pro	Asn	Thr	Cys	Cys	His
				85					90					95	
Phe	Trp	Leu	Met	Val	Trp	Gln	Gln	Lys	Thr	Lys	Ala	Val	Val	Met	Leu
			100					105					110		
Asn	Arg	Ile	Val	Glu	Lys	Glu	Ser	Val	Lys	Cys	Ala	Gln	Tyr	Trp	Pro
		115						120				125			
Thr	Asp	Asp	Gln	Glu	Met	Leu	Phe	Lys	Glu	Thr	Gly	Phe	Ser	Val	Lys
	130					135					140				
Leu	Leu	Ser	Glu	Asp	Val	Lys	Ser	Tyr	Tyr	Thr	Val	His	Leu	Leu	Gln
145					150					155				160	
Leu	Glu	Asn	Ile	Asn	Ser	Gly	Glu	Thr	Arg	Thr	Ile	Ser	His	Phe	His
				165					170					175	
Tyr	Thr	Thr	Trp	Pro	Asp	Phe	Gly	Val	Pro	Glu	Ser	Pro	Ala	Ser	Phe
		180						185					190		
Leu	Asn	Phe	Leu	Phe	Lys	Val	Arg	Glu	Ser	Gly	Ser	Leu	Asn	Pro	Asp
	195					200						205			
His	Gly	Pro	Ala	Val	Ile	His	Cys	Ser	Ala	Gly	Ile	Gly	Arg	Ser	Gly
	210					215					220				
Thr	Phe	Ser	Leu	Val	Asp	Thr	Cys	Leu	Val	Leu	Met	Glu	Lys	Gly	Asp
225					230					235				240	
Asp	Ile	Asn	Ile	Lys	Gln	Val	Leu	Leu	Asn	Met	Arg	Lys	Tyr	Arg	Met
			245					250						255	
Gly	Leu	Ile	Gln	Thr	Pro	Asp	Gln	Leu	Arg	Phe	Ser	Tyr	Met	Ala	Ile
		260					265						270		
Ile	Glu	Gly	Ala	Lys	Cys	Ile	Lys	Gly	Asp	Ser	Ser	Ile	Gln	Lys	Arg
	275						280					285			
Trp	Lys	Glu	Leu	Ser	Lys	Glu	Asp	Leu	Ser	Pro	Ala	Phe	Asp	His	Ser
	290					295					300				
Pro	Asn	Lys	Ile	Met	Thr	Glu	Lys	Tyr	Asn	Gly	Asn	Arg	Ile	Gly	Leu
305					310					315				320	
Glu	Glu	Glu	Lys	Leu	Thr	Gly	Asp	Arg	Cys	Thr	Gly	Leu	Ser	Ser	Lys
			325					330						335	
Met	Gln	Asp	Thr	Met	Glu	Glu	Asn	Ser	Glu	Ser	Ala	Leu	Arg	Lys	Arg
		340						345					350		
Ile	Arg	Glu	Asp	Arg	Lys	Ala	Thr	Thr	Ala	Gln	Lys	Val	Gln	Gln	Met
	355						360					365			
Lys	Gln	Arg	Leu	Asn	Glu	Asn	Glu	Arg	Lys	Arg	Lys	Arg	Pro	Arg	Leu
	370					375					380				
Thr	Asp	Thr													
385															

<210> 169

<211> 79

<212> PRT

<213> Unknown

<220>

<223> Catalytic domain region

<400> 169

Phe	Asn	Asn	Glu	Thr	Arg	Ile	Ile	Tyr	Gln	Phe	His	Tyr	Lys	Asn	Trp
1				5				10					15		
Pro	Asp	His	Asp	Val	Pro	Ser	Ser	Ile	Asp	Pro	Ile	Leu	Gln	Leu	Ile
		20					25					30			
Trp	Asp	Met	Arg	Cys	Tyr	Gln	Glu	Asp	Asp	Cys	Val	Pro	Ile	Cys	Ile
	35						40					45			

His Cys Ser Ala Gly Cys Gly Arg Thr Gly Val Ile Cys Ala Val Asp
 50 55 60
 Tyr Thr Trp Met Leu Leu Lys Asp Gly Ile Ile Pro Lys Asn Phe
 65 70 75

<210> 170
 <211> 79
 <212> PRT
 <213> Unknown

<220>
 <223> Catalytic domain region

<400> 170
 Phe Gln Asn Glu Ser Arg Arg Leu Tyr Gln Phe His Tyr Val Asn Trp
 1 5 10 15
 Pro Asp His Asp Val Pro Ser Ser Phe Asp Ser Ile Leu Asp Met Ile
 20 25 30
 Ser Leu Met Arg Lys Tyr Gln Glu His Glu Asp Val Pro Ile Cys Ile
 35 40 45
 His Cys Ser Ala Gly Cys Gly Arg Thr Gly Ala Ile Cys Ala Ile Asp
 50 55 60
 Tyr Thr Trp Asn Leu Leu Lys Ala Gly Lys Ile Pro Glu Glu Phe
 65 70 75

<210> 171
 <211> 79
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 171
 Phe Gln Lys Glu Ser Arg Ser Val Tyr Gln Leu Gln Tyr Met Ser Trp
 1 5 10 15
 Pro Asp Arg Gly Val Pro Ser Ser Pro Asp His Met Leu Ala Met Val
 20 25 30
 Glu Glu Ala Arg Arg Leu Gln Gly Ser Gly Pro Glu Pro Leu Cys Val
 35 40 45
 His Cys Ser Ala Gly Cys Gly Arg Thr Gly Val Leu Cys Thr Val Asp
 50 55 60
 Tyr Val Arg Gln Leu Leu Leu Thr Gln Met Ile Pro Pro Asp Phe
 65 70 75

<210> 172
 <211> 82
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 172
 Asp Asn Gly Asp Leu Ile Arg Glu Ile Trp His Tyr Gln Tyr Leu Ser

166

```

      1           5           10           15
Trp Pro Asp His Gly Val Pro Ser Glu Pro Gly Gly Val Leu Ser Phe
      20           25           30
Leu Asp Gln Ile Asn Gln Arg Gln Glu Ser Leu Pro His Ala Gly Pro
      35           40           45
Ile Ile Val His Cys Ser Ala Gly Ile Gly Arg Thr Gly Thr Ile Ile
      50           55           60
Val Ile Asp Met Leu Met Glu Asn Ile Ser Thr Lys Gly Leu Asp Cys
65           70           75           80
Asp Ile

```

<210> 173
 <211> 82
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

```

<400> 173
Gly Gln Gly Asn Thr Glu Arg Thr Val Trp Gln Tyr His Phe Arg Thr
      1           5           10           15
Trp Pro Asp His Gly Val Pro Ser Asp Pro Gly Gly Val Leu Asp Phe
      20           25           30
Leu Glu Glu Val His His Lys Gln Glu Ser Ile Met Asp Ala Gly Pro
      35           40           45
Val Val Val His Cys Ser Ala Gly Ile Gly Arg Thr Gly Thr Phe Ile
      50           55           60
Val Ile Asp Ile Leu Ile Asp Ile Ile Arg Glu Lys Gly Val Asp Cys
65           70           75           80
Asp Ile

```

<210> 174
 <211> 75
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

```

<400> 174
Val His Glu Ile Arg Glu Ile Arg Gln Phe His Phe Thr Gly Trp Pro
      1           5           10           15
Asp His Gly Val Pro Tyr His Ala Thr Gly Leu Leu Gly Phe Val Arg
      20           25           30
Gln Val Lys Ser Lys Ser Pro Pro Ser Ala Gly Pro Leu Val Val His
      35           40           45
Cys Ser Ala Gly Ala Gly Arg Thr Gly Cys Phe Ile Val Ile Asp Ile
      50           55           60
Met Leu Asp Met Ala Glu Arg Glu Gly Val Val
65           70           75

```

<210> 175

<211> 75
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 175
 Tyr Asn Glu Ile Arg Glu Val Lys Gln Phe His Phe Thr Gly Trp Pro
 1 5 10 15
 Asp His Gly Val Pro Tyr His Ala Thr Gly Leu Leu Ser Phe Ile Arg
 20 25 30
 Arg Val Lys Leu Ser Asn Pro Pro Ser Ala Gly Pro Ile Val Val His
 35 40 45
 Cys Ser Ala Gly Ala Gly Arg Thr Gly Cys Tyr Ile Val Ile Asp Ile
 50 55 60
 Met Leu Asp Met Ala Glu Arg Glu Gly Val Val
 65 70 75

<210> 176
 <211> 75
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 176
 Tyr His Glu Ile Arg Glu Leu Arg Leu Phe His Phe Thr Ser Trp Pro
 1 5 10 15
 Asp His Gly Val Pro Cys Tyr Ala Thr Gly Leu Leu Gly Phe Val Arg
 20 25 30
 Gln Val Lys Phe Leu Asn Pro Pro Glu Ala Gly Pro Ile Val Val His
 35 40 45
 Cys Ser Ala Gly Ala Gly Arg Thr Gly Cys Phe Ile Ala Ile Asp Thr
 50 55 60
 Met Leu Asp Met Ala Glu Asn Glu Gly Val Val
 65 70 75

<210> 177
 <211> 75
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 177
 Ser Ser Glu Lys Arg Glu Val Arg Gln Phe Gln Phe Thr Ala Trp Pro
 1 5 10 15
 Asp His Gly Val Pro Glu His Pro Thr Pro Phe Leu Ala Phe Leu Arg
 20 25 30
 Arg Val Lys Thr Cys Asn Pro Pro Asp Ala Gly Pro Met Val Val His
 35 40 45
 Cys Ser Ala Gly Val Gly Arg Thr Gly Cys Phe Ile Val Ile Asp Ala
 50 55 60

Met Leu Glu Arg Ile Lys His Glu Lys Thr Val
 65 70 75

<210> 178
 <211> 75
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 178
 Ser Ser Glu Lys Arg Glu Val Arg Gln Phe Gln Phe Thr Ala Trp Pro
 1 5 10 15
 Asp His Gly Val Pro Glu Tyr Pro Thr Pro Phe Leu Ala Phe Leu Arg
 20 25 30
 Arg Val Lys Thr Cys Asn Pro Pro Asp Ala Gly Pro Ile Val Val His
 35 40 45
 Cys Ser Ala Gly Val Gly Arg Thr Gly Cys Phe Ile Val Ile Asp Ala
 50 55 60
 Met Leu Glu Arg Ile Lys Pro Glu Lys Thr Val
 65 70 75

<210> 179
 <211> 75
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 179
 Ser Ser Glu Lys Arg Glu Leu Arg Gln Phe Gln Phe Met Ala Trp Pro
 1 5 10 15
 Asp His Gly Val Pro Glu Tyr Pro Thr Pro Ile Leu Ala Phe Leu Arg
 20 25 30
 Arg Val Lys Ala Cys Asn Pro Leu Asp Ala Gly Pro Met Val Val His
 35 40 45
 Cys Ser Ala Gly Val Gly Arg Thr Gly Cys Phe Ile Val Ile Asp Ala
 50 55 60
 Met Leu Glu Arg Met Lys His Glu Lys Thr Val
 65 70 75

<210> 180
 <211> 79
 <212> PRT
 <213> Unknown

<220>
 <223> Catalytic domain region

<400> 180
 Asp Met Thr Asn Arg Lys Pro Gln Arg Leu Ile Thr Gln Phe His Phe
 1 5 10 15
 Thr Ser Trp Pro Asp Phe Gly Val Pro Phe Thr Pro Ile Gly Met Leu

		20						25					30				
Lys	Phe	Leu	Lys	Lys	Val	Lys	Ala	Cys	Asn	Pro	Gln	Tyr	Ala	Gly	Ala		
		35					40					45					
Ile	Val	Val	His	Cys	Ser	Ala	Gly	Val	Gly	Arg	Thr	Gly	Thr	Phe	Val		
	50					55					60						
Val	Ile	Asp	Ala	Met	Leu	Asp	Met	Met	His	Thr	Glu	Arg	Lys	Val			
65					70					75							

<210> 181
 <211> 78
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

Pro	Asp	Gly	Cys	Lys	Ala	Pro	Arg	Leu	Val	Ser	Gln	Leu	His	Phe	Thr		
1				5				10					15				
Ser	Trp	Pro	Asp	Phe	Gly	Val	Pro	Phe	Thr	Pro	Ile	Gly	Met	Leu	Lys		
			20					25				30					
Phe	Leu	Lys	Lys	Val	Lys	Thr	Leu	Asn	Pro	Val	His	Ala	Gly	Pro	Ile		
		35				40					45						
Val	Val	His	Cys	Ser	Ala	Gly	Val	Gly	Arg	Thr	Gly	Thr	Phe	Ile	Val		
	50					55				60							
Ile	Asp	Ala	Met	Met	Ala	Met	Met	His	Ala	Glu	Gln	Lys	Val				
65					70					75							

<210> 182
 <211> 82
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

Gln	Lys	Gly	Asn	Pro	Lys	Gly	Arg	Gln	Asn	Glu	Arg	Val	Val	Ile	Gln		
1				5				10					15				
Tyr	His	Tyr	Thr	Gln	Trp	Pro	Asp	Met	Gly	Val	Pro	Glu	Tyr	Ala	Leu		
			20					25				30					
Pro	Val	Leu	Thr	Phe	Val	Arg	Arg	Ser	Ser	Ala	Ala	Arg	Met	Pro	Glu		
		35				40						45					
Thr	Gly	Pro	Val	Leu	Val	His	Cys	Ser	Ala	Gly	Val	Gly	Arg	Thr	Gly		
	50					55					60						
Thr	Tyr	Ile	Val	Ile	Asp	Ser	Met	Leu	Gln	Gln	Ile	Lys	Asp	Lys	Ser		
65					70					75					80		
Thr	Val																

<210> 183
 <211> 79
 <212> PRT
 <213> unknown

<220>

<223> Catalytic domain region

<400> 183

```

Ser Gln Lys Gly Arg Pro Ser Gly Arg Val Val Thr Gln Tyr His Tyr
 1              5              10              15
Thr Gln Trp Pro Asp Met Gly Val Pro Glu Tyr Ser Leu Pro Val Leu
      20              25              30
Thr Phe Val Arg Lys Ala Ala Tyr Ala Lys Arg His Ala Val Gly Pro
      35              40              45
Val Val Val His Cys Ser Ala Gly Val Gly Arg Thr Gly Thr Tyr Ile
      50              55              60
Val Leu Asp Ser Met Leu Gln Gln Ile Gln His Glu Gly Thr Val
65              70              75

```

<210> 184

<211> 77

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 184

```

Lys Glu Lys Ala Thr Gly Arg Glu Val Thr His Ile Gln Phe Thr Ser
 1              5              10              15
Trp Pro Asp His Gly Val Pro Glu Asp Pro His Leu Leu Leu Lys Leu
      20              25              30
Arg Arg Arg Val Asn Ala Phe Ser Asn Phe Phe Ser Gly Pro Ile Val
      35              40              45
Val His Cys Ser Ala Gly Val Gly Arg Thr Gly Thr Tyr Ile Gly Ile
      50              55              60
Asp Ala Met Leu Glu Gly Leu Glu Ala Glu Asn Lys Val
65              70              75

```

<210> 185

<211> 79

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 185

```

Glu Gln Leu Asp Ala His Arg Leu Ile Arg His Phe His Tyr Thr Val
 1              5              10              15
Trp Pro Asp His Gly Val Pro Glu Thr Thr Gln Ser Leu Ile Gln Phe
      20              25              30
Val Arg Thr Val Arg Asp Tyr Ile Asn Arg Ser Pro Gly Ala Gly Pro
      35              40              45
Thr Val Val His Cys Ser Ala Gly Val Gly Arg Thr Gly Thr Phe Ile
      50              55              60
Ala Leu Asp Arg Ile Leu Gln Gln Leu Asp Ser Lys Asp Ser Val
65              70              75

```


<210> 186
 <211> 78
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 186
 Gln Thr Ser Glu Ser His Pro Leu Arg Gln Phe His Phe Thr Ser Trp
 1 5 10 15
 Pro Asp His Gly Val Pro Asp Thr Thr Asp Leu Leu Ile Asn Phe Arg
 20 25 30
 Tyr Leu Val Arg Asp Tyr Met Lys Ser Pro Pro Glu Ser Pro Ile
 35 40 45
 Leu Val His Cys Ser Ala Gly Val Gly Arg Thr Gly Thr Phe Ile Ala
 50 55 60
 Ile Asp Arg Leu Ile Tyr Gln Ile Glu Asn Glu Asn Thr Val
 65 70 75

<210> 187
 <211> 76
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 187
 Asp Glu Met Gln Asp Val Met His Phe Asn Tyr Thr Ala Trp Pro Asp
 1 5 10 15
 His Gly Val Pro Thr Ala Asn Ala Ala Glu Ser Ile Leu Gln Phe Val
 20 25 30
 His Met Val Arg Gln Gln Ala Thr Lys Ser Lys Gly Pro Met Ile Ile
 35 40 45
 His Cys Ser Ala Gly Val Gly Arg Thr Gly Thr Phe Ile Ala Leu Asp
 50 55 60
 Arg Leu Leu Gln His Ile Arg Asp His Glu Phe Val
 65 70 75

<210> 188
 <211> 72
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 188
 Gly Asp Cys Met Thr Val Arg Gln Phe Thr Gly Trp Pro Glu His Gly
 1 5 10 15
 Val Pro Glu Asn Thr Thr Pro Leu Ile His Phe Val Lys Leu Val Arg
 20 25 30
 Thr Ser Arg Ala His Asp Thr Thr Pro Met Val Val His Cys Ser Ala
 35 40 45
 Gly Val Gly Arg Thr Gly Val Phe Ile Ala Leu Asp His Leu Thr Gln

<400> 189																
Arg	Asp	Gly	Gln	Ser	Arg	Thr	Val	Arg	Gln	Phe	Gln	Phe	Thr	Asp	Trp	
1				5					10					15		
Pro	Glu	Gln	Gly	Val	Pro	Lys	Ser	Gly	Glu	Gly	Phe	Ile	Asp	Phe	Ile	
			20					25					30			
Gly	Gln	Val	His	Lys	Thr	Lys	Glu	Gln	Phe	Gly	Gln	Asp	Gly	Pro	Ile	
		35					40					45				
Ser	Val	His	Cys	Ser	Ala	Gly	Val	Gly	Arg	Thr	Gly	Val	Phe	Ile	Thr	
	50					55					60					
Leu	Ser	Ile	Val	Leu	Glu	Arg	Met	Arg	Tyr	Glu	Gly	Val	Val			
65					70					75						

<400> 190															
Arg	Asp	Gly	Gln	Ser	Arg	Thr	Val	Arg	Gln	Phe	Gln	Phe	Thr	Asp	Trp
1				5					10					15	
Pro	Glu	Gln	Gly	Val	Pro	Lys	Ser	Gly	Glu	Gly	Phe	Ile	Asp	Phe	Ile
			20					25					30		
Gly	Gln	Val	His	Lys	Thr	Lys	Glu	Gln	Phe	Gly	Gln	Asp	Gly	Pro	Ile
		35					40					45			
Ser	Val	His	Cys	Ser	Ala	Gly	Val	Gly	Arg	Thr	Gly	Val	Phe	Ile	Thr
	50					55					60				
Leu	Ser	Ile	Val	Leu	Glu	Arg	Met	Arg	Tyr	Glu	Gly	Val	Val		
65					70					75					

```

<400> 191
Arg Asp Gly Gln Ser Arg Thr Ile Arg Gln Phe Gln Phe Thr Asp Trp
 1          5          10          15

```

```

Pro Glu Gln Gly Val Pro Lys Thr Gly Glu Gly Phe Ile Asp Phe Ile
      20      25      30
Gly Gln Val His Lys Thr Lys Glu Gln Phe Gly Gln Asp Gly Pro Ile
      35      40      45
Thr Val His Cys Ser Ala Gly Val Gly Arg Thr Gly Val Phe Ile Thr
      50      55      60
Leu Ser Ile Val Leu Glu Arg Met Arg Tyr Glu Gly Val Val
65      70      75

```

<210> 192
 <211> 77
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

```

<400> 192
Arg Glu Asn Lys Ser Arg Gln Ile Arg Gln Phe His Phe His Gly Trp
 1      5      10      15
Pro Glu Val Gly Ile Pro Ser Asp Gly Lys Gly Met Ile Ser Ile Ile
      20      25      30
Ala Ala Val Gln Lys Gln Gln Gln Gln Ser Gly Asn His Pro Ile Thr
      35      40      45
Val His Cys Ser Ala Gly Ala Gly Arg Thr Gly Thr Phe Cys Ala Leu
      50      55      60
Ser Thr Val Leu Glu Arg Val Lys Ala Glu Gly Ile Leu
65      70      75

```

<210> 193
 <211> 82
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

```

<400> 193
Gln Pro Gln Ala Arg Gln Glu Glu Gln Val Arg Val Val Arg Gln Phe
 1      5      10      15
His Phe His Gly Trp Pro Glu Ile Gly Ile Pro Ala Glu Gly Lys Gly
      20      25      30
Met Ile Asp Leu Ile Ala Ala Val Gln Lys Gln Gln Gln Gln Thr Gly
      35      40      45
Asn His Pro Ile Thr Val His Cys Ser Ala Gly Ala Gly Arg Thr Gly
      50      55      60
Thr Phe Ile Ala Leu Ser Asn Ile Leu Glu Arg Val Lys Ala Glu Gly
65      70      75      80
Leu Leu

```

<210> 194
 <211> 78
 <212> PRT
 <213> unknown

<220>

<223> Catalytic domain region

<400> 194

```

Asn Ser Gly Glu Thr Arg Thr Ile Ser His Phe His Tyr Thr Thr Trp
 1           5           10           15
Pro Asp Phe Gly Val Pro Glu Ser Pro Ala Ser Phe Leu Asn Phe Leu
          20           25           30
Phe Lys Val Arg Glu Ser Gly Ser Leu Asn Pro Asp His Gly Pro Ala
          35           40           45
Val Ile His Cys Ser Ala Gly Ile Gly Arg Ser Gly Thr Phe Ser Leu
          50           55           60
Val Asp Thr Cys Leu Val Leu Met Glu Lys Gly Asp Asp Ile
65           70           75

```

<210> 195

<211> 81

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 195

```

Thr Thr Gln Glu Thr Arg Glu Ile Leu His Phe His Tyr Thr Thr Trp
 1           5           10           15
Pro Asp Phe Gly Val Pro Glu Ser Pro Ala Ser Phe Leu Asn Phe Leu
          20           25           30
Phe Lys Val Arg Glu Ser Gly Ser Leu Ser Pro Glu His Gly Pro Val
          35           40           45
Val Val His Cys Ser Ala Gly Ile Gly Arg Ser Gly Thr Phe Cys Leu
          50           55           60
Ala Asp Thr Cys Leu Leu Leu Met Asp Lys Arg Lys Asp Pro Ser Ser
65           70           75           80
Val

```

<210> 196

<211> 89

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 196

```

Glu Glu Arg Gln Lys Arg Gln Val Thr His Phe Gln Phe Leu Ser Trp
 1           5           10           15
Pro Asp Tyr Gly Val Pro Ser Ser Ala Ala Ser Leu Ile Asp Phe Leu
          20           25           30
Arg Val Val Arg Asn Gln Gln Ser Leu Ala Val Ser Asn Met Gly Ala
          35           40           45
Arg Ser Lys Gly Gln Cys Pro Glu Pro Pro Ile Val Val His Cys Ser
          50           55           60
Ala Gly Ile Gly Arg Thr Gly Thr Phe Cys Ser Leu Asp Ile Cys Leu

```

65 70 75 80
Ala Gln Leu Glu Glu Leu Gly Thr Leu
 85

<210>	197
<211>	77
<212>	PRT
<213>	unknown

<220>
<223> Catalytic domain region

<400> 197															
Gln	Thr	Gln	Glu	Thr	Arg	Thr	Leu	Thr	Gln	Phe	His	Phe	Leu	Ser	Trp
1				5					10					15	
Pro	Ala	Glu	Gly	Thr	Pro	Ala	Ser	Thr	Arg	Pro	Leu	Leu	Asp	Phe	Arg
			20					25					30		
Arg	Lys	Val	Asn	Lys	Cys	Tyr	Arg	Gly	Arg	Ser	Cys	Pro	Ile	Ile	Val
		35					40					45			
His	Cys	Ser	Asp	Gly	Ala	Gly	Arg	Thr	Gly	Thr	Tyr	Ile	Leu	Ile	Asp
50						55					60				
Met	Val	Leu	Asn	Arg	Met	Ala	Lys	Gly	Val	Lys	Glu	Ile			
65					70					75					

<210>	198
<211>	77
<212>	PRT
<213>	Unknown

<220>
<223> Catalytic domain region

<400> 198															
Gln	Thr	Asn	Glu	Thr	Arg	Thr	Val	Thr	Gln	Phe	His	Phe	Leu	Ser	Trp
1				5					10					15	
Tyr	Asp	Arg	Gly	Val	Pro	Ser	Ser	Ser	Arg	Ser	Leu	Leu	Asp	Phe	Arg
			20					25					30		
Arg	Lys	Val	Asn	Lys	Cys	Tyr	Arg	Gly	Arg	Ser	Cys	Pro	Ile	Ile	Val
		35				40						45			
His	Cys	Ser	Asp	Gly	Ala	Gly	Arg	Ser	Gly	Thr	Tyr	Val	Leu	Ile	Asp
	50					55					60				
Met	Val	Leu	Asn	Lys	Met	Ala	Lys	Gly	Ala	Lys	Glu	Ile			
65					70					75					

<210>	199
<211>	86
<212>	PRT
<213>	unknown

<220>
<223> Catalytic domain region

<400> 199
Lys Arg Lys Asp Ser Arg Thr Val Tyr Gln Tyr Gln Tyr Thr Asn Trp
1 5 10 15

```

Ser Val Glu Gln Leu Pro Ala Glu Pro Lys Glu Leu Ile Ser Met Ile
      20      25      30
Gln Val Val Lys Gln Lys Leu Pro Gln Lys Asn Ser Ser Glu Gly Asn
      35      40      45
Lys His His Lys Ser Thr Pro Leu Leu Ile His Cys Arg Asp Gly Ser
      50      55      60
Gln Gln Thr Gly Ile Phe Cys Ala Leu Leu Asn Leu Leu Glu Ser Ala
65      70      75      80
Glu Thr Glu Glu Val Val
      85

```

<210> 200
 <211> 78
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

```

<400> 200
Gln Gly Ser His Thr Gln His Val Lys His Tyr Trp Tyr Thr Ser Trp
 1      5      10      15
Pro Asp His Lys Thr Pro Asp Ser Ala Gln Pro Leu Leu Gln Leu Met
      20      25      30
Leu Asp Val Glu Glu Asp Arg Leu Ala Ser Gln Gly Arg Gly Pro Val
      35      40      45
Val Val His Cys Ser Ala Gly Ile Gly Arg Thr Gly Cys Phe Ile Ala
50      55      60
Thr Ser Ile Gly Cys Gln Gln Leu Lys Glu Glu Gly Val Val
65      70      75

```

<210> 201
 <211> 79
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

```

<400> 201
Ser Gly Thr Glu Glu Arg Gly Leu Lys His Tyr Trp Phe Thr Ser Trp
 1      5      10      15
Pro Asp Gln Lys Thr Pro Asp Arg Ala Pro Pro Leu Leu His Leu Val
      20      25      30
Arg Glu Val Glu Glu Ala Ala Gln Gln Gly Pro His Cys Ala Pro
      35      40      45
Ile Ile Val His Cys Ser Ala Gly Ile Gly Arg Thr Gly Cys Phe Ile
50      55      60
Ala Thr Ser Ile Cys Cys Gln Gln Leu Arg Gln Glu Gly Val Val
65      70      75

```

<210> 202
 <211> 86
 <212> PRT
 <213> unknown

<220>

<223> Catalytic domain region

<400> 202

```

Leu Ser Gly Gln Glu Arg Thr Val Trp His Leu Gln Tyr Thr Asp Trp
 1           5           10           15
Pro Asp His Gly Cys Pro Glu Asp Val Gln Gly Phe Leu Ser Tyr Leu
      20           25           30
Glu Glu Ile Gln Ser Val Arg Arg His Thr Asn Ser Met Leu Glu Gly
      35           40           45
Thr Lys Asn Arg His Pro Pro Ile Val Val His Cys Ser Ala Gly Val
      50           55           60
Gly Arg Thr Gly Val Leu Ile Leu Ser Glu Leu Met Ile Tyr Cys Leu
65           70           75           80
Glu His Asn Glu Lys Val
      85

```

<210> 203

<211> 85

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 203

```

Leu Thr Gly Gln Glu Arg Thr Val Trp His Leu Gln Tyr Thr Asp Trp
 1           5           10           15
Pro Glu His Gly Cys Pro Glu Asp Leu Lys Gly Phe Leu Ser Tyr Leu
      20           25           30
Glu Glu Ile Gln Ser Val Arg Arg His Thr Asn Ser Thr Ser Asp Pro
      35           40           45
Gln Ser Pro Asn Pro Pro Leu Leu Val His Cys Ser Ala Gly Val Gly
      50           55           60
Arg Thr Gly Val Val Ile Leu Ser Glu Ile Met Ile Ala Cys Leu Glu
65           70           75           80
His Asn Glu Val Leu
      85

```

<210> 204

<211> 76

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 204

```

Glu Lys Asn Glu Ser Arg Pro Leu Thr Gln Ile Gln Tyr Ile Ala Trp
 1           5           10           15
Pro Asp His Gly Val Pro Asp Asp Ser Ser Asp Phe Leu Asp Phe Val
      20           25           30
Cys His Val Arg Asn Lys Arg Ala Gly Lys Glu Glu Pro Val Val Val
      35           40           45
His Cys Ser Ala Gly Ile Gly Arg Thr Gly Val Leu Ile Thr Met Glu

```

50		55		60							
Thr	Ala	Met	Cys	Leu	Ile	Glu	Cys	Asn	Gln	Pro	Val
65					70					75	

<210> 205
 <211> 75
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 205
 Gln Thr Gly Glu Glu His Thr Val Thr His Leu Gln Tyr Val Ala Trp
 1 5 10 15
 Pro Asp His Gly Ile Pro Asp Asp Ser Ser Asp Phe Leu Glu Phe Val
 20 25 30
 Asn Tyr Val Arg Ser Leu Arg Val Asp Ser Glu Pro Val Leu Val His
 35 40 45
 Cys Ser Ala Gly Ile Gly Arg Thr Gly Val Leu Val Thr Met Glu Thr
 50 55 60
 Ala Met Cys Leu Thr Glu Arg Asn Leu Pro Ile
 65 70 75

<210> 206
 <211> 74
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 206
 Gln Thr Arg Glu Val Arg His Ile Ser His Leu Asn Phe Thr Ala Trp
 1 5 10 15
 Pro Asp His Asp Thr Pro Ser Gln Pro Asp Asp Leu Leu Thr Phe Ile
 20 25 30
 Ser Tyr Met Arg His Ile His Arg Ser Gly Pro Ile Ile Thr His Cys
 35 40 45
 Ser Ala Gly Ile Gly Arg Ser Gly Thr Leu Ile Cys Ile Asp Val Val
 50 55 60
 Leu Gly Leu Ile Ser Gln Asp Leu Asp Phe
 65 70

<210> 207
 <211> 24
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 207
 Gly Gly Arg Val Phe Val His Cys Gln Ala Gly Ile Ser Arg Ser Ala
 1 5 10 15

Thr Ile Cys Leu Ala Tyr Leu Met
20

<210> 208
<211> 24
<212> PRT
<213> unknown

<220>
<223> Catalytic domain region

<400> 208
Arg Gly Arg Val Leu Val His Cys Gln Ala Gly Ile Ser Arg Ser Ala
1 5 10 15
Thr Ile Cys Leu Ala Tyr Leu Met
20

<210> 209
<211> 24
<212> PRT
<213> unknown

<220>
<223> Catalytic domain region

<400> 209
Asn Cys Gly Val Leu Val His Cys Leu Ala Gly Ile Ser Arg Ser Val
1 5 10 15
Thr Val Thr Val Ala Tyr Leu Met
20

<210> 210
<211> 24
<212> PRT
<213> unknown

<220>
<223> Catalytic domain region

<400> 210
Asn Cys Gly Val Leu Val His Cys Leu Ala Gly Val Ser Arg Ser Val
1 5 10 15
Thr Val Thr Val Ala Tyr Leu Met
20

<210> 211
<211> 24
<212> PRT
<213> unknown

<220>
<223> Catalytic domain region

<400> 211

180

Gly Gly Lys Val Leu Val His Cys Glu Ala Gly Ile Ser Arg Ser Pro
 1 5 10 15
 Thr Ile Cys Met Ala Tyr Leu Met
 20

<210> 212
 <211> 24
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 212
 Asn Gly Cys Val Leu Val His Cys Leu Ala Gly Ile Ser Arg Ser Ala
 1 5 10 15
 Thr Ile Ala Ile Ala Tyr Ile Met
 20

<210> 213
 <211> 24
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 213
 Lys Cys Gly Val Leu Val His Cys Leu Ala Gly Ile Ser Arg Ser Val
 1 5 10 15
 Thr Val Thr Val Ala Tyr Leu Met
 20

<210> 214
 <211> 24
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 214
 Gly Gly Arg Val Leu Val His Cys Gln Ala Gly Ile Ser Arg Ser Ala
 1 5 10 15
 Thr Ile Cys Leu Ala Tyr Leu Ile
 20

<210> 215
 <211> 24
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 215

Ser	Cys	Gln	Val	Ile	Val	His	Cys	Leu	Ala	Gly	Ile	Ser	Arg	Ser	Ala
1				5					10					15	
Thr	Ile	Ala	Ile	Ala	Tyr	Ile	Met								
			20												

<210> 216

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 216

Gly	His	Ile	Val	Tyr	Val	His	Cys	Asn	Ala	Gly	Val	Gly	Arg	Ser	Thr
1				5					10					15	
Ala	Ala	Val	Cys	Gly	Trp	Leu	Gln								
			20												

<210> 217

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 217

Asn	Gly	Arg	Val	Leu	Val	His	Cys	Arg	Glu	Gly	Tyr	Ser	Arg	Ser	Pro
1				5					10					15	
Thr	Leu	Val	Ile	Ala	Tyr	Leu	Met								
			20												

<210> 218

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 218

Gly	Glu	Lys	Val	Leu	Val	His	Gly	Asn	Ala	Gly	Ile	Ser	Arg	Ser	Ala
1				5					10					15	
Ala	Phe	Val	Ile	Ala	Tyr	Ile	Met								
			20												

<210> 219

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 219

Gly	Ser	Val	Ile	Leu	Ile	Phe	Ser	Thr	Gln	Gly	Ile	Ser	Arg	Ser	Cys
1				5					10					15	
Ala	Ala	Ile	Ile	Ala	Tyr	Leu	Met								
				20											

<210> 220

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 220

Ser	Gly	Lys	Val	Leu	Val	Ser	Ser	Glu	Met	Gly	Ile	Ser	Arg	Ser	Ala
1				5					10					15	
Val	Leu	Val	Val	Ala	Tyr	Leu	Met								
				20											

<210> 221

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 221

Gly	Gly	Ala	Cys	Leu	Val	Tyr	Cys	Lys	Asn	Gly	Arg	Ser	Arg	Ser	Ala
1				5					10					15	
Ala	Val	Cys	Thr	Ala	Tyr	Leu	Met								
				20											

<210> 222

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 222

Asn	Gly	Arg	Val	Leu	Val	His	Cys	Gln	Ala	Gly	Ile	Ser	Arg	Ser	Gly
1				5					10					15	
Thr	Asn	Ile	Leu	Ala	Tyr	Leu	Met								
				20											

<210> 223

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 223

Asn	His	Val	Ala	Ala	Ile	His	Cys	Lys	Ala	Gly	Lys	Gly	Arg	Thr	Gly
1				5					10					15	
Val	Met	Ile	Cys	Ala	Tyr	Leu	Leu								
			20												

<210> 224

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 224

Glu	Asn	Ile	Val	Ala	Ile	His	Cys	Lys	Gly	Gly	Thr	Asp	Arg	Thr	Gly
1				5					10					15	
Thr	Met	Val	Cys	Ala	Phe	Leu	Ile								
			20												

<210> 225

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 225

Glu	Asn	Ile	Val	Ala	Ile	His	Cys	Lys	Gly	Gly	Lys	Gly	Arg	Thr	Gly
1				5					10					15	
Thr	Met	Val	Cys	Ala	Leu	Leu	Ile								
			20												

<210> 226

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 226

Glu	Asn	Ile	Val	Val	Ile	His	Cys	Lys	Gly	Gly	Lys	Gly	Arg	Thr	Gly
1				5					10					15	
Thr	Met	Val	Cys	Ala	Cys	Leu	Ile								
			20												

<210> 227

<211> 24
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 227
 Glu Asn Ile Val Val Ile His Cys Lys Gly Gly Lys Gly Arg Thr Gly
 1 5 10 15
 Thr Met Val Cys Ala Cys Leu Ile
 20

<210> 228
 <211> 24
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 228
 Tyr Arg Lys Thr Leu Ile His Cys Tyr Gly Gly Leu Gly Arg Ser Cys
 1 5 10 15
 Leu Val Ala Ala Cys Leu Leu Leu
 20

<210> 229
 <211> 25
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 229
 Lys Ser Ser Val Leu Val His Cys Ser Asp Gly Trp Asp Arg Thr Ala
 1 5 10 15
 Gln Leu Thr Ser Leu Ala Met Leu Met
 20 25

<210> 230
 <211> 25
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 230
 Gln Arg Pro Val Leu Val His Cys Ser Asp Gly Trp Asp Arg Thr Pro
 1 5 10 15
 Gln Ile Val Ala Leu Ala Lys Leu Leu
 20 25

<210> 231
<211> 24
<212> PRT
<213> unknown

<220>
<223> Catalytic domain region

<400> 231
Gly Cys Cys Val Ala Val His Cys Val Ala Gly Leu Gly Arg Ala Pro
1 5 10 15
Val Leu Val Ala Leu Ala Leu Ile
20

<210> 232
<211> 24
<212> PRT
<213> unknown

<220>
<223> Catalytic domain region

<400> 232
Gly Ser Cys Val Ala Val His Cys Val Ala Gly Leu Gly Arg Ala Pro
1 5 10 15
Val Leu Val Ala Leu Ala Leu Ile
20

<210> 233
<211> 24
<212> PRT
<213> unknown

<220>
<223> Catalytic domain region

<400> 233
Asp Lys Leu Ile Gly Val His Cys Thr His Gly Leu Asn Arg Thr Gly
1 5 10 15
Tyr Leu Ile Cys Arg Tyr Leu Ile
20

<210> 234
<211> 24
<212> PRT
<213> unknown

<220>
<223> Catalytic domain region

<400> 234
His Lys Asn Cys Val Val His Cys Met Asp Gly Arg Ala Ala Ser Ala
1 5 10 15
Val Ala Val Cys Ser Phe Leu Cys

20

<210> 235
<211> 25
<212> PRT
<213> unknown

<220>
<223> Catalytic domain region

<400> 235
Thr Lys Ser Val Leu Phe Val Cys Leu Gly Asn Ile Cys Arg Ser Pro
1 5 10 15
Ile Ala Glu Ala Val Phe Arg Lys Leu
20 25

<210> 236
<211> 24
<212> PRT
<213> unknown

<220>
<223> Catalytic domain region

<400> 236
Glu Gly Ala Ile Ala Val His Cys Lys Ala Gly Leu Gly Arg Thr Gly
1 5 10 15
Thr Leu Ile Ala Cys Tyr Ile Met
20

<210> 237
<211> 25
<212> PRT
<213> unknown

<220>
<223> Catalytic domain region

<400> 237
Arg Val Ile Leu Ile Phe His Cys Glu Phe Ser Ser Glu Arg Gly Pro
1 5 10 15
Arg Met Cys Arg Phe Ile Arg Glu Arg
20 25

<210> 238
<211> 24
<212> PRT
<213> unknown

<220>
<223> Catalytic domain region

<400> 238
His Gly Ala Thr Leu Val His Cys Ala Ala Gly Val Ser Arg Ser Ala

187

1	5	10	15
Thr	Leu Cys Ile	Ala Tyr	Leu Met
	20		

<210> 239
 <211> 24
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 239			
Gln	Gly Arg Thr	Leu Leu His Cys	Ala Ala Gly Val Ser Arg Ser Ala
1	5	10	15
Ala	Leu Cys Leu	Ala Tyr	Leu Met
	20		

<210> 240
 <211> 24
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 240			
Gly	Glu Ser Cys	Leu Val His Cys	Leu Ala Gly Val Ser Arg Ser Val
1	5	10	15
Thr	Leu Val Ile	Ala Tyr	Ile Met
	20		

<210> 241
 <211> 24
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 241			
Asp	Gly Val Val	Leu Val His Cys	Asn Ala Gly Val Ser Arg Ala Ala
1	5	10	15
Ala	Ile Val Ile	Gly Phe	Leu Met
	20		

<210> 242
 <211> 24
 <212> PRT
 <213> unknown

<220>
 <223> Catalytic domain region

<400> 242

Gly	Arg	Ser	Val	Leu	Val	His	Cys	His	Ala	Gly	Val	Ser	Arg	Ser	Val
1				5					10					15	
Ala	Ile	Ile	Thr	Ala	Phe	Leu	Met								
			20												

<210> 243

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 243

Gly	Lys	Cys	Val	Tyr	Val	His	Cys	Lys	Ala	Gly	Arg	Ser	Arg	Ser	Ala
1				5					10					15	
Thr	Met	Val	Ala	Ala	Tyr	Leu	Ile								
			20												

<210> 244

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 244

Thr	Gly	Arg	Val	Leu	Val	His	Cys	Ala	Met	Gly	Val	Ser	Arg	Ser	Ala
1				5					10					15	
Thr	Leu	Val	Leu	Ala	Phe	Leu	Met								
			20												

<210> 245

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 245

Gln	Gly	Leu	Thr	Leu	Leu	His	Cys	Met	Ala	Gly	Val	Ser	Arg	Ser	Ala
1				5					10					15	
Ser	Leu	Cys	Leu	Ala	Tyr	Leu	Met								
			20												

<210> 246

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 246

Gly	Gly	Lys	Ile	Leu	Val	His	Cys	Ala	Val	Gly	Val	Ser	Arg	Ser	Ala
1				5					10					15	
Thr	Leu	Val	Leu	Ala	Tyr	Leu	Met								
				20											

<210> 247

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 247

Gly	Lys	Gly	Leu	Leu	Ile	His	Cys	Gln	Ala	Gly	Val	Ser	Arg	Ser	Ala
1				5					10					15	
Thr	Ile	Val	Ile	Ala	Tyr	Leu	Met								
				20											

<210> 248

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 248

Gly	Glu	Ala	Val	Gly	Val	His	Cys	Ala	Leu	Gly	Phe	Gly	Arg	Thr	Gly
1				5					10					15	
Thr	Met	Leu	Ala	Cys	Tyr	Leu	Val								
				20											

<210> 249

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 249

His	Ser	Lys	Cys	Leu	Val	His	Cys	Lys	Met	Gly	Val	Ser	Arg	Ser	Ala
1				5					10					15	
Ser	Thr	Val	Ile	Ala	Tyr	Ala	Met								
				20											

<210> 250

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 250

Gly	Ser	Lys	Cys	Leu	Val	His	Cys	Lys	Met	Gly	Val	Ser	Arg	Ser	Ala
1				5					10					15	
Ser	Thr	Val	Ile	Ala	Tyr	Ala	Met								
			20												

<210> 251

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 251

His	Ser	Lys	Ile	Leu	Val	His	Cys	Val	Met	Gly	Arg	Ser	Arg	Ser	Ala
1				5					10					15	
Thr	Leu	Val	Leu	Ala	Tyr	Leu	Met								
			20												

<210> 252

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 252

Gly	Thr	His	Val	Leu	Val	His	Cys	Lys	Met	Gly	Val	Ser	Arg	Ser	Ala
1				5					10					15	
Ala	Thr	Val	Leu	Ala	Tyr	Ala	Met								
			20												

<210> 253

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 253

Asn	Gly	Cys	Val	Leu	Val	His	Cys	Leu	Ala	Gly	Ile	Ser	Arg	Ser	Ala
1				5					10					15	
Thr	Ile	Ala	Ile	Ala	Tyr	Ile	Met								
			20												

<210> 254

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 254

Gly Ala Lys Val Leu Val His Cys Val Val Gly Val Ser Arg Ser Ala
1 5 10 15

Thr Leu Val Leu Ala Tyr Leu Met
20

<210> 255

<211> 24

<212> PRT

<213> unknown

<220>

<223> Catalytic domain region

<400> 255

Gly Gly Asn Cys Leu Val His Cys Phe Ala Gly Ile Ser Arg Ser Thr
1 5 10 15

Thr Ile Val Thr Ala Tyr Val Met
20